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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

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SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

[*Continued from* p. 165.]

Treatment.

General.—In a circular letter from the Office of the Surgeon General of the U.S. Army (p. 96) on the suppression and treatment of malaria, the routine use of pamaquin (plasmoquine) is not advised. Mepacrine does not affect the flight capacity of aviators, and is the drug of choice for suppressive therapy, in doses of 0·6 gm. or 0·4 gm. each week. For treatment of an attack, mepacrine may be given in 0·2 gm. doses every 6 hours for five doses, followed by 0·1 gm. thrice daily for six days. For quinine the suppressive dose is 10 grains daily, the curative dose 15 grains thrice daily for two days, followed by 10 grains thrice daily for five days. [In hyperendemic areas it is probable that suppression requires 0·6 or 0·7 gm. mepacrine weekly, and that 10 grains of quinine each day is ineffective.]

NELSON-JONES (p. 537) has compared three standard courses of treatment of subtertian malaria in the Gold Coast. He found that quinine 30 grains daily for seven days, followed by quinine 20 grains daily for seven days was far preferable to a quinine-plasmoquine or a quinine-mepacrine-plasmoquine course in that complete recovery was quicker and progressive ill-health less common. There is no evidence that plasmoquine reduces the relapse rate of *P. falciparum* infections, and the author would prefer to abandon the use of this drug.

RAPER *et al.* (p. 647) have investigated the effect of treatment lasting only three days, on malaria in immune and non-immune Africans. An immune African, for the purpose of this experiment, was one who was brought up in a district in which the transmission season exceeded six months in the year. Three different courses of treatment were compared, one with quinine, one with mepacrine and one with both. It is concluded that immune Africans with malaria need not be admitted to hospital, but that for non-immunes admission is desirable. All three courses were satisfactory, the combined course being the best.

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1944, v. 41. References to the abstracts are given under the names of the authors quoted and the page on which the abstracts are printed.

CURD (p. 101) has compiled, from the extensive literature available, a table of the activity of a large number of drugs in malaria of man, monkeys and birds.

KOHLSCHÜTTER *et al.* (p. 454) have estimated the lethal doses of pamaquin, certuna, mepacrine and quinine for fowls, and describe the pathological appearances produced by these doses. They emphasize, however, that the symptoms produced in birds by the toxic action of these drugs are different from those produced in man.

Quinine.—LOWE (p. 997) makes the point that unnecessary delay in instituting treatment for malaria is criminal. He gives higher initial doses of quinine in *P. falciparum* than in *P. vivax* infections, and prefers oral administration if possible. If quinine must be injected, the intravenous, rather than the intramuscular, route should be adopted.

From experiments in birds, BECKMAN and SMITH (p. 545) conclude that treatment with quinine given every two hours is more effective than that given less frequently, but in the same total dosage. This would indicate that continuous administration in man might justifiably be tried.

MCGUIRE (p. 539) has found that quinine sulphate solution can be used for intramuscular injection. It is no more prone than the dihydrochloride solution to cause abscess. [But, as the salt is dissolved in an acid solution, one would expect more muscle necrosis than with a solution more nearly neutral.]

In a discussion of malignant and atypical malaria, KNEEDLER (p. 450) advocates treatment with quinine (intravenously or intramuscularly) in the early stages, followed by mepacrine. There is never any indication for intravenous mepacrine, since only small doses are advisable by this route, but if necessary it can be given intramuscularly.

YOUNG and MACADEN (p. 724) condemn large intravenous doses of quinine as a first treatment of cerebral malaria, preferring an immediate intramuscular injection, followed, 4–6 hours later, by a small intravenous injection of 3–6 grains. This may be repeated to a total of three injections.

ROGAN (p. 921) treats cerebral malaria by intravenous quinine given slowly, and repeats the injections (up to a total dosage of 30 grains in 24 hours) until recovery from coma takes place. GILLETT (p. 538) has successfully used intravenous pentothal sodium to control patients with cerebral malaria of violent maniacal type. Intravenous quinine was given while the patients were under the influence of this narcosis.

KELSEY *et al.* (p. 11) have determined the distribution of quinine in the tissues of the fowl. There is great variation in the blood concentration after oral administration, and when repeated doses are given, most of the drug is detoxified each day. Details are given in the original abstract. KELSEY *et al.* (p. 923) show that when quinine is incubated with certain animal tissues it is converted into substances which no longer have the solubility or fluorescent characteristics of quinine. BURTON, KELSEY and OLDHAM (p. 260) have shown that quinine is present in the foetus of the pregnant rabbit after it has been given to the mother; that the placenta has some power to impede the passage of quinine; that the power of the liver of the pregnant rabbit to destroy quinine is not so great as that of the non-pregnant rabbit. Certain animal tissues destroy quinine *in vitro*, and oxygen is required in this process; there is great variation in the activity of the different tissues in this respect. The agent responsible for this destruction is termed quinine oxidase and the loss of liver activity in the destruction of quinine during pregnancy appears to be due to lack of this enzyme rather than to some inhibitory mechanism.

KEOGH and SHAW (p. 1003) have sought to elucidate the action of quinine in malaria, and as a result of their experiments they conclude that there is a

physiological antagonism between quinine and calcium, and that quinine interferes with growth and reproduction of the malaria parasite by reducing the amount of calcium available in red cells.

JOHNSON and SCHNEYER (p. 923) have investigated the quinine inhibition of bacterial luminescence, with a view to throwing some light on the action of quinine on malaria parasites. The paper should be studied in original.

HOWIE and MURRAY-LYON (p. 185) have studied the Tanret reaction in relation to the ingestion of quinine. In 100 patients undergoing quinine treatment seven failed to give a positive reaction and five were positive at irregular intervals. These men responded poorly to the treatment, but reacted well to injection of quinine. In 53 healthy persons the reaction became strongly positive within five hours of taking quinine, though there was considerable individual variation, and it was negative again after 24 hours. It is recommended that quinine dosage should be regulated for each person by the results of the Tanret test.

BARANGER and THOMAS (p. 103) have shown that the total alkaloids of *Cinchona* from West Africa are as effective as quinine against *P. relictum* in canaries, but that the total alkaloids from which quinine has been extracted have poor therapeutic effect. JOHANNESSOHN (p. 727) describes Prochinin, a mixture of cinchonine, cinchonidine and quinidine, which has been used successfully by the Germans in malaria. GALPERIN (p. 825) discusses the antimalarial action of quinoline compounds.

Alkaloids from the bark of *Alstonia* (widely distributed in Australia), though resembling quinine in many respects, were found by KEOGH and SHAW (p. 365) to have little antimalarial effect in animals.

Mepacrine and Pamaquin.—HAWKING (p. 1005) has examined the local effects of mepacrine dihydrochloride, mepacrine methanesulphonate and quinine dihydrochloride, when injected intramuscularly. The damage caused to muscle by the two salts of mepacrine is far from negligible, though probably less extensive than that caused by quinine. The oral route is, therefore, to be preferred to intramuscular injection, if this is possible. Mepacrine should not be given subcutaneously or intravenously.

KIRZON (p. 261) treats his cases of severe malaria by injection of mepacrine intramuscularly, the dose being 0·3 gm. in 10–12 cc. water. The usual course is one injection each day for 3–5 days. Blood transfusion is also beneficial. FERNANDEZ MARIÑA (p. 1004) gives details of a course of treatment in which mepacrine is given intravenously as well as by mouth. The method is safe [but compare HAWKING, above].

EPSTEIN (p. 451) has adopted an initial large dose of mepacrine (0·5–0·6 gm. on the first day) in his treatment of benign and malignant tertian malaria. This produces earlier termination of fever than 0·3 gm. on the first day. In each case the drug is continued in daily doses of 0·3 gm.

KONJ and YAKOVLEVA (p. 922) have adopted a prolonged course of mepacrine and pamaquin treatment, in an area of central Russia in which *P. vivax* is the common parasite, for the prevention of relapse, and show that this has been more successful than a shorter course. Mepacrine is given in daily doses of 0·2 gm. for periods of 3–5 days, alternating with 10-day intervals, throughout the period when relapses occur (April–June). The later courses include pamaquin in 0·04 gm. doses.

The toxicity of mepacrine has been investigated by several workers :—

KAHLER (p. 451) describes two cases of unusual reactions to mepacrine; in comment, HAWKING points out that such happenings are rare. WRIGHT and LILLIE (p. 99) give an account of the toxic effects produced by heavy doses of mepacrine and sulphadiazine, but in comment HAWKING remarks that these doses far exceed any used clinically.

In a well-controlled investigation LOUGHLIN *et al.* (p. 186) showed that American mepacrine (atabrine) is no more toxic than the German product, and that, in the usual suppressive doses, it does not normally cause important toxic reactions.

WAELSCH and NACHMANSOHN (p. 649) postulate that the toxic action of mepacrine may be due to the fact that it inhibits choline esterase, the substance which destroys acetyl choline, and that the result is similar to stimulation of the vagus.

SCUDI *et al.* (p. 728) show that with doses of one-half the LD50, mepacrine was fatal to a high proportion of rats which had received no food for 12–36 hours, especially if their previous diet had been deficient in protein. With this dose there was evidence of severe gastro-intestinal irritation, and inhibition of liver function, increased by fasting.

SCUDI and HAMLIN (p. 728) show that the toxicity of mepacrine for rats can be mitigated by a diet rich in protein and poor in fat. In dogs on normal diet, toxic symptoms were produced by continued high dosage of mepacrine, and an increase in plasma fibrinogen, indicating destruction of liver tissue, was observed. In lower dosage, liver damage could be produced if the animals were on low-protein diet, but controls on high protein were not affected.

REGSTED *et al.* (p. 649) have shown that continuous administration of mepacrine to rats on ordinary diets may affect their growth and condition if in high dosage, and may intensify any ill-effect due to the diet if this is deficient in protein or riboflavin. But on a low-protein, low-choline diet the addition of mepacrine seemed to have a protective effect.

PICK and HUNTER (p. 924) have shown, by electrical means, that mepacrine has a depressant action on the brain of the cat. In comment, HAWKING points out that, in man, mental disturbances due to mepacrine are rare unless large doses are given.

BOCK and OESTERLIN (p. 545) describe their observations on fluorescent substances in relation to a number of parasites. Specifically active substances are absorbed by special parts of the parasites (blepharoplast, etc.), whereas absorption of fluorescent but inactive substances is more general, and the fluorescence is not produced except in relatively high concentration. Monkeys infected with malaria were treated with mepacrine, which was visible in the parasites under the fluorescence microscope before morphological changes took place in them. The authors consider that the action of mepacrine is directly upon the parasites.

BRODIE and UDENFRIEND (p. 453) describe a method of estimating mepacrine in biological fluids and tissues, by which amounts as low as 0·1 μgm. may be estimated, with an error of less than 5 per cent. A simpler but less accurate method is also described.

ANNEGERS *et al.* (p. 98) have examined the retention and excretion of mepacrine in animals; details should be sought in the original abstract. SCUDI and HAMLIN (p. 262) have also investigated the distribution and excretion of mepacrine in experimental animals, but for details the original should be consulted. SCUDI and JELINEK (p. 452) describe the urinary excretion products of mepacrine; the paper is technical and should be consulted in original by those interested.

SHISHLIAEVA-MATOVA (p. 819) has found that a systematic treatment with mepacrine and pamaquin, both therapeutic and suppressive, was not very effective in eradicating infection on a collective farm in a hyperendemic area of Russia; and concludes that for effective control where the vector mosquito population is high, drug treatment should be reinforced by anti-larval measures.

MANSON-BAHR (p. 1003) does not think that pamaquin should be given in the average case of subtertian malaria, and refers to the need to give intravenous quinine slowly in cerebral malaria.

MANN (p. 100) reports a case in which haemoglobinuria occurred after the patient had been treated for malaria with quinine, mepacrine and pamaquin (plasmoquine). The author attributes this to the plasmoquine, which apparently has two toxic effects—the production of haemagglutinins which are not specific to the patient's red cells, and of a haemolysin and a toxin with direct action on the renal tubules.

Other Drugs.—JOHNSON (p. 100) has treated a few patients, inoculated with *P. malariae*, with sulphadiazine in daily doses of 4 gm. or less, to a total dosage of 24–48 gm. The results were satisfactory but three of the 13 patients had relapses, which were controlled by second courses of sulphadiazine.

LOWE (p. 825) shows that neoarsphenamine and mapharside have some therapeutic action against *P. vivax*, but not against *P. falciparum* or *P. malariae*.

Suppressive Treatment.

PARROT, *et al.* (p. 539) have carried out experiments on suppressive drug treatments in the native population of highly malarious places in Algeria, where *A. maculipennis labranchiae* is the vector. Under the conditions of the experiment [in which, no doubt, the state of immunity of the people had its importance] it was found that administration of 0·2 gm. mepacrine twice each week was as effective as daily administration (except on Sundays) of 0·4 gm. quinine. Both drugs diminished the reservoirs of *P. vivax* and *P. malariae*, but neither completely suppressed *P. falciparum* during the season of heavy transmission. There were no toxic results from mepacrine, except that immediate vomiting was often provoked in infants. Suppressive treatment cannot replace other anti-malarial measures.

LEVENSON *et al.* (p. 10) report on a campaign of mass chemoprophylaxis with mepacrine which was apparently successful in reducing greatly the incidence of malaria in the region of Archangel. The dosage was 0·2 or 0·3 gm. daily for periods of 2–5 days, continued, at intervals of 10 days, through the spring and summer. In comment BUXTON points out that these authors report *P. vivax* and *P. falciparum* in a region further north than any hitherto recorded in Russia. In particular, *P. falciparum* has, so far, only been known in the centre and south of Russia.

TALBOT (p. 97), in a description of malaria in an outlying military base [presumably in the Far East] where antilarval measures were impossible, remarks that he does not advise the use of suppressive medication except in an area of actual combat, in an endemic area.

CLARK (p. 9) has for 10 years been attempting to control malaria in Panama by the administration of anti-malarial drugs to all persons in whom parasites are found at the monthly surveys. In this way the incidence of malaria may be somewhat reduced, but it has not been possible to eradicate it or to prevent relapse. More recent work, done on the basis of survey every two months, has confirmed the previous conclusions. He (p. 924) contributes another report on control of malaria in Panama by giving treatment to persons found to be harbouring malaria parasites. The parasite rates in those given mepacrine were rather higher than in those given quinine, but for various reasons complete surveys and complete treatment were impossible. The author remarks that general opinion seems to underestimate the importance of relapse in *P. falciparum* infections.

Control.

A fourth year's study of the efficacy of spray-killing adult mosquitoes (*A. culicifacies*) has confirmed previous findings in South India. RUSSELL *et al.* (p.

456) report that it reduces malaria transmission to a marked degree. Houses, animal sheds and buildings were sprayed with a pyrethrum preparation, usually at weekly intervals, during the transmission season. Results, estimated by spleen and parasite rates, were very good in comparison with control villages, and it is noted that the villagers appreciate the benefits. The cost per person varied from 3 to 7½ annas.

ANNECKE (p. 457) has experimented with various repellents, and concludes that plain citronella oil still holds first place among those tested, provided that it is applied every three hours, but that a cream containing naphthalene and a concentrated extract of pyrethrum was almost as good.

WILSON and MELVILLE (p. 263) describe the general measures taken to reduce the incidence of malaria in the forces serving in the East African Command. The conditions in the different areas varied from continuous transmission to seasonal transmission of different degrees, and in some places there was no transmission. The anti-malaria organization is described, and it is stated that since it became adequate in size, incidence has usually been brought down, in a few weeks, to less than 100 per cent. per annum. Malaria-mindedness in the troops is very important, and so is camp siting. Track discipline is emphasized, since rain-filled car tracks can produce enormous numbers of *A. gambiae.* The proper use of protective clothing and nets is a matter on which discipline should be strict; repellents have not been much used, and head nets have not been successful in practice. Spray-killing of adult mosquitoes in the quarters and in other likely resting places is essential, and is always practicable, in military malaria control. Anti-larval measures are now regarded as a routine in almost all circumstances, and malaria can be controlled under apparently most unpromising conditions; oiling, of course, is largely used, but drainage may often reduce the areas to be oiled. Suppressive drug treatment has not been used to a great extent; it has not often been necessary. The authors finally stress the importance of applying all anti-malaria measures to the maximum possible extent, and give information which demonstrates the success that may be achieved.

RIBBANDS (p. 925) points out that camp siting, even in areas where there are no places free from anophelines, is a most important anti-malaria measure. One factor is the distance of the camp (of uninfected persons) from the nearest infected human population, and the risk is negligible if 5 miles intervene, and small at 2 miles. Risk is greater if breeding occurs between the village and the camp. Small infected communities are dangerous in that there are fewer persons for the mosquitoes to attack than in larger centres. If complete removal of the infected community is impossible (as it usually is), partial removal is worse than useless unless it is the children (the richest reservoir) who are removed. In choosing camp sites, higher ground should be given preference.

COVELL (p. 646) has contributed a comprehensive review of the prevention and treatment of malaria in war in the light not only of actual wartime experience, but also of the researches carried out in peace. The review cannot adequately be summarized, and readers should refer to the original.

BUTLER (p. 361) describes malaria control in a South Pacific Island where the only vector was *A. punctulatus moluccensis*, which breeds freely in rain pools, road ruts, etc., and in semi-shaded margins of pools and streams. The measures taken were not new, but all forms of control were used and emphasis was laid on malaria discipline. Very little use, however, was made of insecticides and repellents. Suppressive treatment with mepacrine was useful while control was being organized; no toxic effects were seen from a weekly dosage of 0·4 gm.

FREEBORN (p. 729) writes of the danger of large-scale introduction of malaria into the United States by troops who will return from the various theatres of war. Anti-anopheline measures are being undertaken in many States, and

particular attention is to be paid to the environs of general hospitals, in which, presumably, there will be comparatively heavy concentrations of parasite carriers.

DE ANDRADE (p. 1007) describes the important part played by Paris green in the eradication of *A. gambiae* from Brazil. The best results were given by a type whose particles were about 2 microns in diameter. There was no case of poisoning of animals or man, in spite of the widespread use of Paris green.

MURRAY and KNUTSON (p. 1007) report on the good results obtained by dusting with Paris green from aeroplanes, once each week in the summer, on the breeding of *A. quadrimaculatus* in the Potomac river. ZUMPT (p. 265) gives, in some detail, his experiences with aircraft as a means of scattering Paris green or oil, for the control of anopheline larvae. Details of the amounts, diluents and results should be sought in the original abstract. In general, the Paris green experiments were successful, but the attempts to use oil were abandoned.

NESTERWODSKAJA and LUBINSKI (p. 102) have confirmed the high toxicity of phenothiazine to mosquito larvae, especially *Anopheles*. In field trials at 12–13°C., with dosages of 7 and 14 oz. per acre, all *Anopheles* larvae had disappeared in 48 hours. Phenothiazine is toxic to fish, but is practically harmless to mammals [presumably in the doses likely to be ingested under these conditions. In high doses phenothiazine may be very toxic].

NEWBOLD (p. 11) describes a self-clearing drainage outlet from coastal swamps which have a ground level about that of high tide. This has successfully been used in Trinidad and Grenada. Details are given in the original abstract. COCHRANE and NEWBOLD (p. 102) have achieved satisfactory results in the prevention of breeding of *A. argyritarsis* in a stream in Grenada by the installation of an automatic flushing siphon. They observe that although this mosquito has never been proved a vector, it is strongly suspected.

The deliberate increase in salinity of coastal lagoons in the West Indies is effective in controlling the breeding of *A. albimanus* provided that the salinity reaches 75 per cent. of that of sea water. HURLBUT (p. 266) shows that increased salinity not only reduces the proportion of females which lay eggs, but also the proportion of eggs which hatch out.

In the *Bol. Oficina Sanitaria Panamericana* (p. 102) is an account of the anti-malaria campaign in the Republic of Panama, where *A. albimanus* is by far the most important vector.

COVELL and SINGH (p. 455) give an account of an outbreak of malaria which occurred in Delhi in 1942 as a result of exceptionally heavy rainfall in that year. The previous epidemic had occurred 9 years earlier, and the general immunity was consequently low. In general, the permanent anti-malarial engineering work already done was effective in limiting the outbreak, but there were formed, nevertheless, extensive sheets of water ideal for the breeding of *A. culicifacies*. The chief emergency measure adopted was the spray-killing of adult mosquitoes, which seemed to be effective.

ADISUBRAMANIAM and VEDAMANIKKAM (p. 458) have found that antilarval measures against *A. fluviatilis* may reasonably be limited to breeding places within 1,000 to 1,500 feet of the dwellings they are designed to protect.

CUNNINGHAM-VAN SOMEREN (p. 1006) writes of the use of elephant grass in protecting the banks of drainage canals against erosion and damage.

RECTOR (p. 650) has described the method of blasting ditches in wet or marshy land by the use of dynamite, a method which was used successfully in anti-malaria work in Palestine some years ago.

A group of Russian workers (RAEVSKY *et al.*, p. 541) have carried out considerable research on the question of prevention of malaria by interposing, between human habitations and mosquito breeding places, the cowsheds and other animal houses belonging to the communities. They observe that this

form of prevention is possible in the Soviet Union because animals are common property, and can be fully controlled. Evidence is produced that, by proper placing of the animals, the spleen rate and other signs of infection can be greatly reduced, and that the mosquitoes (races of *A. maculipennis*) are diverted from man to the animals. In some places this form of malaria control is the only one possible, but it is advised that zooprophylaxis should be reinforced by suppressive treatment in hyperendemic areas. The barrier consists of a row of animal houses, not less than 200 metres from the human settlement; they should be 45–50 metres apart, and their doors should be on the leeward side. Between the barrier and the village there should be vegetation. Attraction to mosquitoes is through their sense of smell, and is proportionate to the surface area of the animal. Cows and buffaloes are the most attractive; horses are not so effective as cattle.

Malaria of Monkeys and Birds.

MAIER and COGGESHALL (p. 826) have investigated the immunity conferred on monkeys by infection with *P. knowlesi*, which was controlled (so as to prevent death) and maintained as a chronic infection for varying periods of time. The infections were rendered chronic by timely doses of quinine, and were terminated by sulphathiazole. From infections lasting only a few days no immunity was conferred, but from those lasting several weeks, or longer, partial immunity persisted, after sterilization of the infection, for periods up to one year. The duration of the chronic infection influenced the degree of immunity, but not, apparently, its duration.

ROY and MUKERJEE (p. 103) have shown that during the severe phases of *P. knowlesi* infection the complement in monkey blood is greatly reduced.

SIDDONS and BOSE (p. 826) report that a butyl-acridine derivative has a powerful action against *P. knowlesi*; this may be comparable with the action of mepacrine (which is an amyl-acridine derivative).

RODHAIN (p. 544) has succeeded in passing the quartan-like parasite of chimpanzees (*P. rodhaini*) to man, and now takes the view that it probably is *P. malariae*.

BISHOP and GILCHRIST (p. 731) have succeeded in collecting sporozoites of *P. gallinaceum* by allowing infected *Aëdes aegypti* to feed through a membrane on heparinized blood. The sporozoites so obtained may be used for chemotherapeutic experiments.

DAVEY (p. 365) discusses the phases of development of *P. gallinaceum*. In his view the sporozoites leave the blood to enter the tissues (primary tissue phase) thence they re-enter the blood or tissues (secondary tissue phase, represented by the exo-erythrocytic schizonts). These secondary phase forms are capable of indefinite schizogony, but whereas the primary tissue phase is probably common to all malaria parasites, the secondary tissue phase has been described definitely only in *P. gallinaceum* and *P. elongatum*, and probably in *P. circumflexum* and *P. cathemerium*. A true causal prophylactic would act on the sporozoites or the parasites of the primary phase.

ADLER and TCHERNOMORETZ (pp. 103, 366, 458) have shown that exo-erythrocytic forms of *P. gallinaceum* can produce merozoites which invade red cells and develop into gametocytes.

HAWKING (p. 732) has successfully cultivated exo-erythrocytic schizonts of *P. gallinaceum* by means of tissue cultures of spleen, liver, marrow and brain of infected chicks.

ZAIN and WOLF (p. 104) have investigated the influence of X-rays on *P. gallinaceum*.

RUSSELL *et al.* (p. 104) have studied the spleen volume in fowls infected with *P. gallinaceum*.

SCHENG (p. 366) has tested quinine, atebrin and plasmoquine against exo-erythrocytic forms of *P. cathemerium in vitro*, in concentrations much greater than can be attained *in vivo*. The results indicate that exo-erythrocytic forms are very resistant to these drugs.

WOLFSON (p. 104) has studied infection of ducks with a strain of *P. cathemerium*. A series of rapid passages has increased the intensity of the infection, which may now prove suitable for chemotherapeutic research.

REICHENOW and MUDROW (p. 190) have traced in great detail the development of *P. praecox* in birds, with special reference to the formation of exo-erythrocytic and erythrocytic parasites, and of gametocytes. The exo-erythrocytic forms are derived from those parasites which divide into large merozoites, the erythrocytic forms from cells which produce much smaller merozoites, and the proportion of the latter to the former is quickly increased, so that after the fifth cycle no further endothelial development takes place. Gametocytes are produced by the first merozoites which enter red cells, so that sexual differentiation has already taken place at that stage.

REDMOND and PRATHER (p. 267) have compared the infections produced in pigeons and canaries by *P. relictum* [*P. praecox*]; there was little difference so far as the parasite was concerned.

MANWELL (p. 268) has studied infections in ducks with four species, *P. circumflexum*, *P. elongatum*, *P. nucleophilum* and *P. relictum matutinum*. The duck is a good host for each of these, and may be used for chemotherapeutic studies.

JACOBS (p. 458) has shown that an antigen containing saline-insoluble residues of *P. lophurae*, injected into ducks, conferred a degree of protection against subsequent infection, which was increased if staphylococcus toxoid was added to each dose just before administration. It is thought that the useful malarial antigens are of the nature of insoluble haptens.

By experiments on ducks infected with *P. lophurae* and treated with quinine, WALETZKY and BROWN (p. 188) have been unable to exclude the possibility that a metabolic product of quinine is the therapeutic agent.

HEWITT and RICHARDSON (p. 188) have obtained evidence that, in ducks infected with *P. lophurae*, quinine, mepacrine and pamaquin attack the parasite directly; the mechanism of their action is not clear, but there is no evidence that they stimulate phagocytosis or other immune reactions.

BARRETTO (p. 732) reports that exo-erythrocytic forms of *P. juxtanucleare* have been found.

PATTON and METCALFE (p. 546) have shown that fluorescent dyes can be used satisfactorily for the staining of *Haemoproteus* of quails.

SEELER *et al.* (p. 651) confirm previous work which indicated that deprivation of biotin was deleterious in bird malaria.

THOMPSON and HUFF (p. 827) give an account of a new species of *Plasmodium* from a Mexican lizard, and report that exo-erythrocytic forms of this parasite have been found. They also describe the other plasmodia found in Central American lizards.

MANWELL and EDGETT (p. 189) report on the importance of certain factors in the low temperature preservation of malaria parasites. For details the original abstract should be consulted. *Charles Wilcocks.*

MALARIA.

i. SABROSKY, C. W. & USINGER, R. L. **Nomenclature of the Human Malaria Parasites.** *Science.* 1944, Sept. 1, 190–92.

ii. HEMMING, F. **Generic and Specific Trivial Names of the Tertian and Quartan Malaria Parasites.** [Correspondence.] *Nature.* 1944, Dec. 2, 701. Also in *Brit. Med. J.* 1945, Jan. 20, 85.

i. In their opening remarks the authors of this note quote from STILES (1928) " the nomenclature of the parasites of malaria in man and birds represents one of the most confusing chapters in the entire history of zoological nomenclature." They refer to the article on this subject by CHRISTOPHERS and SINTON [this *Bulletin*, 1939, v. 36, 390] and concur in the conclusions drawn by these writers. They trace the history of the various names which have been proposed from time to time, beginning with LAVERAN's *Oscillaria* of 1881. They find that, regarded as belonging to a single genus, the names of the three common parasites of man should be *Oscillaria vivax* (Grassi and Feletti, 1890), *O. quartanae* (Celli and Sanfelice, 1891) and *O. malariae* Laveran, 1881. As attempts to introduce these names into medical and zoological literature at this late date would cause the utmost confusion the authors suggest that the International Commission of Zoological Nomenclature legalize (what has already been expressed in Opinion 104 and advocated by CHRISTOPHERS and SINTON) the existing practice of calling the parasites *Plasmodium vivax* (Grassi and Feletti, 1890), *Plasmodium malariae* (Grassi and Feletti, 1890) and *Plasmodium falciparum* (Welch, 1897). [For some reason which does not seem to be in accord with the rules of nomenclature the authors write *Plasmodium malariae* (Feletti and Grassi, 1889, 1890) and *Plasmodium falciparum*, Welch (1897)].

ii. In the second paper, from *Nature*, Francis Hemming, Secretary of the International Commission on Zoological Nomenclature, invites, in connexion with the above discussion, expressions of opinion from specialists concerned in any aspect of the malaria problem. *C. M. Wenyon.*

MACFIE, J. W. S. **Terminology in Malaria.** [Correspondence.] *Brit. Med. J.* 1945, Feb. 3, 163.

In an annotation in the *British Medical Journal* of January 20th, 1945, approval was expressed of a suggestion by the Reporting Committee of the Malaria Commission of the Health Organisation of the League of Nations [*Bull. Health Organisation* (League of Nations), 1940, v. **9**, No. 2, 146]; this was that the specific names of the different malarial parasites should be used to denote the fevers, *e.g.*, *vivax* malaria, *falciparum* malaria, &c. When, however, the author tried recently to use these terms in the commentary of a medical film, it was found that the name *malariae* malaria was almost impossible to enunciate clearly and caused confusion, so the attempt had to be abandoned. The difficulty would be avoided if the fevers were named *vivax*-tertian, *falciparum*-tertian, *ovale*-tertian, and *malariae*-quartan, although these names are nearly as clumsy as the old ones. [See also CHRISTOPHERS & SINTON, this *Bulletin*, 1939, v. 36, 390; SABROSKY & USINGER, above; HEMMING, above; J. NAT. MAL. SOC., this *Bulletin*, 1944, v. 41, 996.]. *J. F. Corson.*

JACKSON, A. V. *Plasmodium ovale* **Malaria; a Report of Two Cases contracted in New Guinea.** *Med. J. Australia.* 1944, Sept. 9, v. 2, No. 11, 278–9.

" *Plasmodium ovale* parasites were found in the blood of two patients at an Australian general hospital in New Guinea. These patients had not previously been in a malarious area, and so presumably the infections were contracted in

New Guinea. *Plasmodium ovale*, which has not hitherto been reported from New Guinea, is a rare parasite and infections by it should only be diagnosed after a very careful examination of several thin blood films taken at different stages of the asexual cycle."

SAMARASINGHE, D. S., PLYASENA, A. K. & RUSTOMJEE, K. J. *P. tenue* **Forms and "Band" Forms of** *P. vivax* **seen in Ceylon during the Epidemic of 1943.** [Abstract.] *J. Malaria Inst. of India.* 1944, June, v. 5, No. 3, 397.

RIBBANDS, C. R. **The Influence of Rainfall, Tides and Periodic Fluctuations on a Population of** *Anopheles melas*, **Theo.** *Bull. Entom. Res.* 1944, Nov., v. 35, Pt. 3, 271–95, 8 figs. [19 refs.]

The author has recently pointed out that *Anopheles gambiae* var. *melas* is in fact more than a melanic variety of *A. gambiae* breeding in sea water, since it differs from the latter in permanent structural and physiological features [this *Bulletin*, 1945, v. 42, 3]. No certain way of distinguishing all adult *A. melas* from *A. gambiae* has been found, since only a variable proportion possess the "*melas*-band" on the terminal white band of the palp. As a result of the distinction referred to, *A. melas* has now been fully recognized as an important vector of malaria in the coastal regions of West Africa.

The experiments described in this paper were carried out near Freetown in Sierra Leone. A map and brief account of the important climatic and geographical features of the district are given. It included two main breeding areas, a brackish grassy breeding area flooded only at high tide (so that in the season of low rainfall it is mainly dry) and a brackish *Avicennia* mangrove breeding area. In the dry season all the water was saline and would support mainly *A. melas*, but in the wet season certain parts of the water were almost fresh, and were capable of supporting *A. gambiae*. Since, however, the percentage of "*melas*-banded" individuals in the population remained more or less constant it was concluded that the population at all times was in fact very largely one of *A. melas*.

Two huts were erected near the grassy breeding area and baited with the same natives throughout the experiments. The mosquitoes were caught by covering the floor of the enclosure with a sheet and spraying out with a pyrethrum spray. The mosquitoes collected on the sheets were counted and the results expressed as an index (number of mosquitoes divided by number of natives per hut). The experiments extended from 10th January to 31st October, 1941.

The general conclusions arrived at after detailed statistical treatment of the results were as follows. Seasonal variation: The average size of the adult population was closely determined by rainfall, but peak populations only occurred 20–30 days after the causative rainfall, and no response was apparent before the lapse of 10 days. Fluctuations in the rainfall level have the greatest effect on the size of the population. The rate of increase in the population after rainfall was very variable, the maximum being 240 per cent. after one eight-day interval, compared with a tenfold increase in a similar period following a high tide in the dry season. Short term fluctuations: There was evidence for the occurrence of peaks in the population of *Anopheles melas* in a cycle of not more than 16 days. Certain of these, occurring in the dry season, were definitely correlated with the occurrence of a high tide seven to nine days previously, in the wet season this correlation was not apparent. Some peaks could be accounted for by previous rainfall, and still others, it is suggested, may be due to the effects of intra-specific competition in the larval environment. It appears that heavy rainfall does not reduce the adult population by direct killing action.

From the practical point of view it can be seen that *A. melas* is an all-the-year round carrier, but the dry season population is only about one-tenth of that of the wet season. Although influenced by tides, the *A. melas* population level was more influenced by rainfall, and sharp increases could follow after a rain storm in any season. In the absence of rain, spring tides were the main cause of the breeding of *A. melas*, and methods of preventing access of high tides to breeding areas would affect control provided that the protected area was adequately drained in the wet season.

In the dry season, when there has been no appreciable rainfall for six weeks, temporary anti-larval measures, such as oiling and Paris green, are only likely to be useful in the four days following maximum spring tides. At other times weekly oiling, or dusting at four-day intervals, is necessary.

W. A. L. David.

LEWIS, D. J. **Observations on *Anopheles gambiae* and other Mosquitoes at Wadi Halfa.** *Trans. Roy. Soc. Trop. Med. & Hyg.*, 1944, Dec., v. 38, No. 3, 215–29, 1 map & 2 figs. [23 refs.]

Wadi Halfa, the most northerly town in the Sudan, is situated near the southern end of the navigable reach of the Nile just north of the second cataract. It is an important town on the Nile route since it has an aerodrome and is a terminus for railway and steamer services. The area concerned in this study is a narrow belt on both sides of the river extending from the cataract to Faras, some 58 km. downstream. The mosquito fauna is represented by but eight of the 22 species common to the zoogeographical regions to the north and south. *Anopheles gambiae* is the only one considered in any detail, although short notes are given on each of the other species.

There are various reasons for giving attention to the position of *A. gambiae* in the Wadi Halfa area: firstly, in order to control malaria in the town itself; secondly, if *A. gambiae* can be exterminated in Egypt, it might be possible to confine it to the area south of Wadi Halfa; thirdly, it might represent a more serious problem if the level of the Aswan Reservoir is increased above its present height, since that would extend the now restricted swampy area due to seepage.

The area is a favourable one for the application of mosquito control measures. Geographically, it is isolated from the east and west by the desert, climatically the low rainfall (0·2 mm. per annum) and low humidity of the atmosphere are unfavourable for mosquito breeding and survival, while the prevailing wind is almost always northerly so that insects emerging in the cataract area have less chance of invading Wadi Halfa. Finally, communications with the surrounding area do not provide a great danger of reinfestation, since boats from the south do not proceed beyond the cataract, and other ships, aircraft and trains are treated with sprays.

The main breeding sites are the pools among the islands of the cataract, the pools on sandy banks in mid stream, and those near the margin of the river. These pools are formed by changes in the water level. Under the prevailing conditions *A. gambiae* would pass from egg to adult in about seven days in summer but might take about one month in winter. Breeding appears to cease between mid-December and mid-April; this is presumably due to the fact that the pools dry up before the larvae complete their development. It appears, in fact, that the species dies out, since it is unlikely that adults would survive for four months at the low prevailing humidity. The April source of *A. gambiae* is probably the cataract, since larvae have been found in December and March, and it is likely that they persist throughout the winter.

The control measures applied consist of oiling, the application of Paris-green, and draining; the larvivorous fish, *Gambusia holbrooki*, is also very successful.

In order to check the spread of infestation from the cataract, it was decided to control a six kilometre stretch of river and adjacent cultivated land extending from the cataract to a point about two kilometres north of Wadi Halfa. The assumption was made that few *A. gambiae* would fly northwards beyond this band, and it appears to have been fully justified; south of the band a malaria outbreak occurred and *A. gambiae* were found breeding in untreated pools, while all but four of the control untreated pools north of the band remained free from *A. gambiae* for ten months. *W. A. L. David.*

MARNEFFE, H. RANQUE, J. & SAUTET, J. Quelques points de la biologie de l'*Anopheles* (*Myzomyia*) *gambiae* dans la vallée moyenne du Niger. [**Points in the Biology of** *A. gambiae* **in the Middle Niger Region.**] *Bull. Soc. Path. Exot.* 1943, July 7, v. 36, Nos. 7–8, 223–6.

The authors have studied the precipitin reaction of the blood in about 250 female *A. gambiae* collected in a variety of environments (indoors and out) in and about Bamako, on the Niger. Domestic animals were common in and about the villages. In 55 per cent. a positive "human" reaction was obtained. The only available serum was anti-human, so that the absence of positive reactions to other mammals is without significance.

In about 150 female *A. gambiae* the maxillary index was fifteen to seventeen. *P. A. Buxton.*

SHAPIRO, J. M., SALITERNIK, Z. & BELFERMAN, S. **Malaria Survey of the Dead Sea Area during 1942, including the Description of a Mosquito Flight Test and its Results.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Nov., v. 38, No. 2, 95–116, 1 map, 1 pl. & 1 chart.

This is an account of investigations carried out to determine the source of *Anopheles* mosquitoes that infested the residential quarters of the Palestine Potash Works situated on the western side of the north shore of the Dead Sea. The observations recorded are of exceptional interest.

A description is given of the topography and meteorology of this desert-like valley 400 metres below sea level. The three anophelines found were *A. sergenti*, *A. multicolor* and *A. superpictus*. During the past 12 years the sea has receded, leaving a high shoreline with brackish water outcrops along the western shoulder of the lake. During a search on this shoreline in the morning, before sunrise, puddles with *Culex* and *A. multicolor* larvae were found. When the place was revisited about 8.30 in the morning these puddles had disappeared and only after the removal of 10 to 15 cm. of gravel was the water with the larvae again disclosed. This nightly rise and daily fall of water level in sea-shore puddles was noted several times during the investigations. The saline content of these puddles was 2·5 per cent. NaCl.

The persistence of *A. sergenti* after all nearby breeding places had been eliminated or controlled, suggested that the mosquitoes were coming from the Feshka swamps, from 4½ to 7½ kilometres south of the nearest Potash Works quarters. These swamps, 1 km. wide from the hills to the sea, are fed by about 50 springs at the foot of the hills; elevations of gravel and coarse sand obstruct the run-off of this spring water. The salinity of the water in the puddles and seepage areas varies from 0·25 to 0·65 per cent. NaCl. In the spring *A. sergenti* (predominating), *A. multicolor* and *A. superpictus* breed there in large numbers. In the autumn breeding in the gravel water outcrops is still more predominantly

A. sergenti, with a very small percentage of *A. superpictus* and *A. multicolor*. *A. sergenti* continued to breed throughout the winter months of 1943.

In order to collect a large number of mosquitoes for a flight test, 14 men spent a November night in the Feshka swamps seated in a circle with legs or thighs and arms bared. The mosquito alighting on the bare skin was taken in a test tube with the aid of a torch, preferably before biting. The mosquitoes thus caught were transferred to cages. By morning 2,600 mosquitoes had been captured, all but 11 being *A. sergenti*. Early in the evening the first mosquitoes to arrive were culicines; after half an hour these disappeared and anophelines came on the scene. The anophelines came in waves throughout the night; the waves were independent of any change of wind; the night was almost windless.

For the flight test the mosquitoes were sprayed with gold dust, a finely powdered bronze preparation. One *A. sergenti* female with specks of gold dust on thorax and abdomen was captured 4·2 kilometres from the place of release, on the second night after release.

Adult *A. sergenti* could be found in very large numbers in caves in the hill-side adjacent to the Feshka swamps. Sometimes male mosquitoes formed 75 per cent. of the total catch. In the Kallia Hotel, at the Potash Works, about half the *A. sergenti* captured were males. Thus in the Dead Sea area male *A. sergenti* disperse for long distances and their presence does not indicate the proximity of breeding places. It is interesting that on several occasions *A. sergenti* were found in the open field near bushes in the early evening, but only when there was no wind or a very slight breeze. This indicates that *A. sergenti* rest in the open on their way to habitations in search of blood.

About 25 female *A. sergenti*, whose thoraces were covered with the pollen of the plant *Anabasis articulata*, were captured at distances of from 1 to 1½ kilometres from the nearest source of this pollen. The authors suggest that a coloured pollen, foreign to the area to be tested, might be a useful method of marking mosquitoes for flight tests.

Mites were found on about 20 to 25 per cent. of the mosquitoes taken in the Feshka caves and on about 3 to 5 per cent. of *A. sergenti* taken in the buildings of the Potash Works. Mites were found mostly on females, but also on males. The mites were identified as Hydrachnidae, fresh water mites of the Thya class. Very extensive search was made for the source of these Hydrachnidae. They were found on three occasions in Feshka waters and nowhere else. This finding is very strong evidence that *A. sergenti* found in the buildings of the Potash Works originated in swamps from 4½ to 8 kilometres away.

Norman White.

BEKLEMISHEV, V. N. & GONTAEVA, A. A. [**Anophelogenous Landscapes of North-West Iran.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 17–32. [In Russian.]

Very little is known regarding the incidence of malaria and the distribution of the mosquito fauna in Iran. In 1941 the authors made a brief survey of the north-western part of the country, with the object of determining the local epidemiological situation, with special reference to the breeding places of anopheline mosquitoes. With Tabriz as the base, the survey was conducted along two routes: one, encircling Lake Urumiya, the other through Mianeh, Zinjan, Kazvin, Resht, Pahlavi, and back. This territory comprises the three main types of landscape of Iran: (1) the low-lying coastal plain of the Caspian Sea, (2) the north-western uplands, and (3) a small area of the central plateau.

The uplands represent an elevated plateau, from 1,000 to 1,800 metres above sea level, with mountain chains rising up to 4,000 metres. Natural vegetation is sparse but considerable areas are taken up by orchards and vineyards, which are under perennial irrigation, and by various food crops (chiefly wheat and rice), which are irrigated only twice a year. The anopheline fauna of this region includes *Anopheles superpictus*, *A. maculipennis maculipennis*, *A. m. sacharovi* and *A. bifurcatus*. Since the antimalarial organization in Iran is undeveloped, and specific treatment of malaria is restricted to wealthier classes, the bulk of the population remains untreated. On account of this the spread of the disease is governed by elemental factors, chiefly depending on the altitude of the locality. In towns situated on the plateau itself (*e.g.*, Kazvin, Tabriz, Rezayeh, Khoi) the position is satisfactory. The low endemicity of malaria in these places is due to the presence of large arable areas with a limited water supply, all the available water being directed from the streams into irrigation canals, in which an intermittent flow is maintained. These conditions determine the small size of anophelogenous water collections with an insignificant mosquito population. However, in towns situated in mountain valleys (*e.g.*, Maragheh, Mianeh, Zinjan) the incidence of malaria is appreciable. Here the areas of arable land are relatively small, but there is an abundant and constant supply of water, which is used lavishly and allowed to overflow, forming standing collections of water which provide numerous suitable breeding places for mosquitoes.

The Caspian coastal area is in complete contrast to the plateau region, most of it representing a submontane plain lying at sea level and intersected by numerous rivers and streams which descend from the mountains, while a considerable area is occupied by the delta of Sefid-Ruda and the country between the rivers is frequently swampy. The climate in the plains is subtropical. Much of the cultivated land is taken up by rice, as well as wheat and other crops, and considerable numbers of cattle are kept. Except for towns, human dwellings are scattered, and apart from rice-fields, there is no irrigation system, but drainage ditches are numerous.

The predominant malaria vectors are *A. maculipennis* and *A. hyrcanus*, while *A. superpictus* is absent. The distribution of mosquitoes is determined largely by the presence of *Gambusia* in most of the rivers and their tributaries, as well as in the canals. Mosquito larvae could not be found in any of these streams, but they breed mainly in closed water collections and in rice fields, from which the larvivorous fish are absent. The authors were unable to obtain exact figures for the incidence of malaria in the areas visited by them, but there seems to be a considerable decrease in the number of cases during the last few years, which is attributed to the spread of the larvivorous fish since their introduction in 1936. [For other records of malaria in Iran, see this *Bulletin*, 1944, v. 41, 637, 638.] *C. A. Hoare.*

BIELOGLAZOV, G. G. [**Anopheles in the East of the Mongolian People's Republic.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 33–6, 1 fig. [In Russian.]

The author reports the wide distribution of *Anopheles maculipennis messeae* throughout the eastern part of the Mongolian People's Republic, where this mosquito occurs along the basins of the rivers Onon, Uldsa, Kerulen and Khalkhin-gol, occupying the alluvial plains within the forest zones, as well as the steppe country, and intermediate landscapes. It is noted that the marked continental climate of this region, with a severe winter, does not prevent the preservation and multiplication of this species of mosquito. A detailed description is given of the geographical and climatic features of the country explored and of the mosquito fauna collected. *C. A. Hoare.*

COVA-GARCÍA, P. Penetración y dispersión en Venezuela de las especies *Anopheles* (*Nyssorhynchus*) *darlingi* y *Anopheles* (*Nyssorhynchus*) *albimanus*. *Rev. Sanidad Asistencia Social.* Caracas. [**Penetration and Dispersion in Venezuela of** *A. darlingi* **and** *A. albimanus*.] 1943, v. 8, No. 3, 467–72, 1 map.

Abstracted in *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 230–31.

RIGDON, R. H. **The Pathological Lesions in the Brain in Malaria.** *Southern Med. J.* 1944, Dec., v. 37, No. 12, 687–94, 7 figs. [35 refs.]

A general review.

OLDFIELD, M. C. **Traumatic Rupture of Malarial Spleen.** *J. Roy. Army. Med. Corps.* 1945, Jan., v. 84, No. 1, 27–8, 1 fig.

WOOD, P. **The Erythrocyte Sedimentation Rate in Infective Hepatitis and in Malaria.** *Brit. Med. J.* 1945, Jan. 6, 9, 1 chart.

The author describes the results of E.S.R. estimations done by the Wintrobe technique in a series of cases of early infective hepatitis and malaria. In 30 among 35 cases of infective hepatitis seen in the first 10 days of the disease the E.S.R. was under 10 mm. in one hour; in none of the cases did it exceed 20 at this stage. It was found to rise slowly and steadily during the period of biliuria, and after the urine was bile-free it fell slowly to normal. In 23 of 32 cases of malaria the E.S.R. was between 20 and 60 mm. in one hour. The author thinks that this test is of considerable value in differentiating the two diseases in their early stages.

In 84 per cent. of 72 measurements on cases of malaria between the 10th and 20th days of the disease the E.S.R. was above 10 mm. in one hour. This helps to differentiate malaria from various short term fevers which may have been treated as clinical malaria, since the latter usually show a normal E.S.R. by the end of the first week. *J. A. R. Miles.*

COLEMAN, Marion B. **Vi Agglutinative Properties for** *Bacterium typhosum* **demonstrated following Infection with Malaria Parasites.** *J. Lab. & Clin. Med.* 1944, Sept., v. 29, No. 9, 916–20. [Summary appears also in *Bulletin of Hygiene.*]

The sera of a high proportion of persons suffering from malaria were found to contain *Bact. typhosum* Vi agglutinins at titres ranging from 1/10 to 1/640. The sera of 23 out of 34 persons who were receiving malaria therapy and of 11 out of 28 persons suffering from naturally acquired malaria were positive. The author also confirmed the increased frequency of Vi agglutinins in the sera of individuals who had received heat killed phenolized typhoid vaccine, especially by the intravenous route. The presence of Vi antibodies was not directly related to the existence of H or O agglutinins.

The possible explanations of the observations are that malaria parasites possess Vi antigen or that the reaction is anamnestic, previously existing Vi agglutinins being re-stimulated by the malarial infection.

J. C. Cruickshank.

RAYMOND, W. D. **The Equivalent Quinine Index and Therapeutic Efficiency of Totaquina.** *East African Med. J.* 1944, Oct., v. 21, No. 10, 291–7.

Since 1942, totaquina has been prepared at Dar-es-Salaam; it contains all the cinchona alkaloids (the so-called Type I totaquina). The composition has

varied somewhat with different batches but three typical batches in 1944 had the composition :—

	Per cent.
Quinine	33–49
Cinchonidine	13–32
Cinchonine	6–10
Quinidine	0·1–1·5
Amorphous alkaloids	14–22
Moisture	2·6–4·5
Ash	2·7–4·1

It is calculated that 1 gm. of this product is equivalent to 0·5–0·58 gm. quinine base ; 1 gm. quinine sulphate is equivalent to 0·75 gm. quinine base. The alkaloids are present as the free bases and before absorption they must be dissolved in the acid gastric juices, converted into bihydrochlorides. Evidence from the literature is quoted to show that totaquina is practically as effective therapeutically as quinine while, apart from a few exceptional batches in past records, it is no more toxic. Assuming that the alkaloids of cinchona, other than quinine, are fairly effective in the treatment of malaria, approximately twice as much active drug can be obtained from local bark as totaquina as would have been available as quinine ; moreover, the yield of total alkaloids per acre from the local species of cinchona is about double that from the species *ledgeriana* preferred by quinine manufacturers. Accordingly, it is urged that totaquina of this type is the most economical and effective means of obtaining the antimalarial action of cinchona bark. *F. Hawking.*

East African Med. J. 1944, Oct., v. 21, No. 10, 289–91. **The Cinchona Alkaloids and Totaquina.** [Editorial : signed D.B.W.]

This is a comment on the paper by Raymond. The extraction of quinine from cinchona bark by orthodox methods is a complicated and therefore costly process, involving two-thirds of the cost of production of quinine. Extraction of the alkaloids *en bloc* is simple and inexpensive. The Dar-es-Salaam totaquina is being sold retail at 2½ shillings per 100 tablets, which is little more than half the retail cost of quinine tablets. Since economic factors play such a large part in the treatment among native populations in the tropics, this aspect is of the greatest importance. The composition of totaquina should be standardized so that a uniform product is available. It should not be regarded as an inferior substitute for quinine, but advantage should be taken of its lower cost to make it more widely available to those who need it. [This re-emphasis on the valuable antimalarial action of the cinchona alkaloids other than quinine is strongly supported by recent unpublished American work.] *F. Hawking.*

Maegraith, B. G., Brown, G. M., Rossiter, R. J., Irvine, K. N., Lees, J. C., Parsons, D. S., Partington, C. N., Rennie, J. L. & Havard, R. E. **Ammonia Excretion and the Clearance of Mepacrine.** [Correspondence.] *Nature.* 1944, Dec. 16, 766.

This is a preliminary notice about an investigation to enable the concentration of mepacrine in the urine to be estimated by examination of the urine. The concentration of mepacrine in the urine is proportional to the concentration of mepacrine in the plasma and to the concentration of ammonia in the urine ; if any two of these quantities are known, the third can be calculated. Accordingly the equation is given

$$PM = \frac{1}{k} \frac{UM}{UNH_3}$$

in which PM is plasma mepacrine in microgm./litres ; UM is urinary mepacrine in microgm./litre ; UNH_3 is urinary ammonia in mgm. nitrogen/100 cc. ;

and $k=2{\cdot}4$. By this means, the concentration of mepacrine in the plasma can be estimated almost as accurately as by direct examination with Masen's method [this *Bulletin*, 1945, v. 42, 8]. Probably the relation between the amount excreted in the urine and the amount of ammonia in the urine holds also for other basic drugs, *e.g.*, quinine.

[Modern work on the use of mepacrine has placed great emphasis on estimation of the concentration of mepacrine in the plasma. Direct estimation of this concentration requires considerable experience and a well equipped laboratory, including a good centrifuge and a delicate fluorimeter. On the other hand, simple methods are now available for the estimation of mepacrine and ammonia in urine using Lovibond discs. The above equation allows estimations of plasma mepacrine to be made in a simple field laboratory with a minimum of equipment.] *F. Hawking.*

HAYMAN, J. M., Jr. **Atabrine Pigmentation of the Sclera.** *Bull. U.S. Army Med. Dept.* 1944, Nov., No. 82, 120–21.

Pigmentation of the skin, especially around the mouth and on the hands and feet, occurs in most people who take 0·6 gm. or more of atabrine [mepacrine] per week. The sclera, however, are usually unaffected, but when staining does occur, it is apt to be mistaken for jaundice. This happened in two persons seen by the author. The coloration was most intense around the limbus, in the part of the sclera exposed in the palpebral fissure, and was fainter towards the fornices; in jaundice the reverse occurs, pigmentation being most intense in the fornices. *J. F. Corson.*

WRIGHT, C. I. & SABINE, Jean C. **The Effect of Atabrine on the Oxygen Consumption of Tissues.** *J. Biol. Chem.* 1944, Sept., v. 155, No. 1, 315–20, 5 figs.

The effect of atebrin [mepacrine], in low concentrations, on the O_2 consumption of rat tissue slices suspended in phosphate-buffered saline, *p*H 7·3, has been studied in the Barcroft apparatus in an atmosphere of oxygen. The drug at first increased the O_2 uptake by liver slices of a well nourished rat, and later inhibited it, while in the case of liver slices from fasted rats the initial stimulation was small or absent. The O_2 consumption by rat brain or kidney slices was also inhibited. [These results are in contrast to those of MARTIN, *et al.*, *J. Pharm. & Exper. Therap.*, 1939, v. 65, 156.] The addition of lactate, pyruvate, citrate, fumarate or malate failed to restore oxygen uptake after treatment of the tissues with atebrin, whereas the addition of succinate caused a sharp rise in its consumption. Atebrin did not interfere with the oxidation of p-phenylene diamine by tissue slices. The drug inhibited the oxidation of *dl*-alanine by d-amino acid oxidase, but the prosthetic group from the enzyme preparation counteracted its effects. The author suggests that the yellow enzyme systems are affected by atebrin. *J. D. Fulton.*

HAAS, E. **The Effect of Atabrine and Quinine on Isolated Respiratory Enzymes.** *J. Biol. Chem.* 1944, Sept., v. 155, No. 1, 321–31, 2 figs. [21 refs.]

In view of the inhibitory action of antimalarial drugs on plasmodial and tissue respiration [this *Bulletin*, 1938, v. 35, p. 711, 1942, v. 39, p. 397, and the preceding abstract (WRIGHT and SABINE)], the effect of atebrin [mepacrine] and quinine on the isolated components of the respiratory enzyme system has been investigated as an aid to the understanding of the mode of action of these drugs. The components of this system are shown in an accompanying figure. The activity

of the various enzymes, as well as their inhibition by atebrin and quinine, were studied with the aid of spectrophotometric and manometric methods. Atebrin was found to inhibit cytochrome oxidase three times as effectively as quinine. The author, however, considered that the inhibition produced even by atebrin in the case of this enzyme was too small to account for its action on malaria parasites. Cytochrome *c* was not inhibited by this drug. Cytochrome reductase consists of a prosthetic group, alloxazine mononucleotide (vitamin B_2 phosphate) along with a specific protein, and is dissociable. Its activity was measured by its rate of reduction of cytochrome *c*, and the inhibitory effect of atebrin on this reaction suggested that the latter reacted with the free protein arising from dissociation of the enzyme complex, for which protein the prosthetic group also competed. An irreversible drug-protein complex is apparently formed whereby respiration is interfered with, a result which is dependent to some extent on temperature, and largely on the concentration of the drug. One molecule of prosthetic group antagonized the action of 500 molecules of atebrin, indicating that the specific protein has a greater affinity for alloxazine mononucleotide than for the drug. The author therefore suggests that certain alloxazine derivatives might prove efficient antimalarials by combining with specific enzyme proteins, and at the same time fail to function as growth or respiratory factors for the malarial parasite. He also suggests that atebrin might be more effective in treatment if excess of vitamin B_2 phosphate were absent from the patient's diet. Atebrin was 12 times as effective as quinine in inhibiting cytochrome reductase. The activity of the prosthetic group (triphosphopyridine nucleotide) in glucose-6-phosphate dehydrogenase was not inhibited by atebrin, while that of the protein part of the complex was inhibited but remained unaffected by quinine. Some experiments suggested that the action of atebrin might alternatively be due to displacement of substrate rather than of the prosthetic group competing with it for enzyme protein. Quinine shows a less marked inhibition of isolated respiratory enzymes or of malaria parasite respiration than does atebrin, and the author believes that the mechanism of action of the two drugs in malaria may not be the same. Attempts to isolate any of the known respiratory catalysts from *P. knowlesi* parasites which had been dried for some time proved unavailing. *J. D. Fulton.*

ALLEN, C. **Diagnosis of Psychotic Symptoms in Atebrin Intoxication.** [Correspondence.] *Brit. Med. J.* 1944, Dec. 23, 831.

Patients who have been given large doses of atebrin for malaria may develop certain mental symptoms—" a florid hypomanic state, sometimes with vague paranoid delusions, often with grandeur " ; visual hallucinations are absent. When this occurs, general paralysis is suspected and a Wassermann test is done and may give a positive result due to malaria. The serious results that may follow such a mistaken diagnosis are obvious. The author recently met with such a case in a man who had returned from North Africa ; his wife was told that her husband was syphilitic and that she and their children were possibly also infected. *J. F. Corson.*

BIRD, W. **Atebrin and Plasmoquine in the Treatment of Benign Tertian Malaria.** [Abstract.] *J. Malaria Inst. of India.* 1944, June, v. 5, No. 3, 395–6.

WEST, J. B. & HENDERSON, A. B. **Plasmochin Intoxication.** *Bull. U.S. Army Med. Dept.* 1944, Nov., No. 82, 87–99, 3 graphs. [Refs. in footnotes.]

A review is given of the literature dealing with the toxic effects of pamaquin (plasmochin). FISCHER and WEISE [this *Bulletin*, 1928, v. 25, 135] considered

that 0·03 gm. daily was the maximum dosage of this drug which should be given. The present paper is based on the treatment of 846 young males, previously infected with *P. falciparum* in a tropical area. Each was given 10 grains (0·67 gm.) quinine sulphate three times daily for three days or until the fever was controlled, and then 0·1 gm. mepacrine three times daily for five days. After a rest period of two days, the patient was given pamaquin 0·01 gm. three times daily for five days. The patients were ambulatory. Twenty-four of the 846 men (2·85 per cent.) had to be readmitted to hospital for what appeared to be pamaquin intoxication. The smallest amount causing toxic symptoms (four patients) was 0·06 gm. The symptom complex consisted of jaundice (20 cases); abdominal pain (19 cases), colicky and recurrent, responding to anti-spasmodics, slowest of all the symptoms to disappear [in five cases it continued for four weeks after the drug was stopped. Could some of this be due to psychological causes?]; anaemia, r.b.c. below 4 million per cmm. (19 cases); headache (16 cases) dull, persistent, occipital, relieved by acetyl salicylate; weakness (14 cases); and dizziness (11 cases). Two cases developed mild toxic psychoses. Liver and spleen were normal, and there was no methaemoglobinaemia. In the blood of 22 patients examined, there was increased icteric index with or without hyperbilirubinaemia. In nine cases the urine contained albumin or bile, sometimes both; in four cases blood was detected by benzidine tests; in six urines examined, urobilinogen was found.

All the patients were taken into hospital and treated by palliative methods including an increased intake of fluid. The time spent in hospital was 7–72 days, average 25 days. The authors consider a dose of 0·01 gm. pamaquin twice daily for two days as sufficient to render the blood non-infective for mosquitoes and to be free from toxic effects.

[The authors give their reasons for believing that these symptoms were due to intoxication by pamaquin rather than to some other cause, but it must be admitted that the latter possibility is difficult to exclude. At a military hospital in England over 200 men with relapses due to *P. vivax* were treated with 10 grains quinine and 0·01 gm. (of base) pamaquin three times daily for 10 days. No toxic symptoms apart from two cases of gastro-intestinal disturbances were observed and the proportion permanently cured by this course was greater than that cured by mepacrine.] *F. Hawking.*

LEITMAN, M. Z. [**Prophylaxis with Acriquine and Plasmocide in an Area of High Malaria Incidence in a Rice-Field Zone of Uzbekistan.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 62–72. [In Russian.]

The author describes the results of mass chemotherapeutic treatment of malaria in a number of settlements of the Tashkent Province (Central Asia), the population of which is engaged in agricultural work, in the vicinity of numerous rice-fields, representing the main mosquito-breeding places in this locality. The prevalent malaria vectors are *Anopheles maculipennis sacharovi* (87·2 per cent.), *A. superpictus* (10·9 per cent.), and an insignificant proportion of *A. pulcherrimus* and *A. hyrcanus*. An examination of 1,595 inhabitants for malaria, in 1938, revealed the following figures: endemic index 43·6, spleen index 40, parasite rate 6·8, Ross's index 2·9. This population was divided into two groups, (1) an experimental group of 838 persons, and (2) a control group of 757, both comprising persons of different sexes and ages in comparable proportions. The first group underwent suppressive treatment with 0·2 gm. acriquine [mepacrine] + 0·04 gm. plasmocide [pamaquin] given daily for two days in succession, followed by an interval of three days (this was the dose for adults, children receiving smaller amounts). This cycle was repeated regularly. In the control group therapeutic treatment with acriquine was applied

to those persons who became infected. Some difficulty was experienced with children under the age of eight, owing to their inability and disinclination to swallow the acrid acriquine tablets. Such cases, as well as refractory adults, were treated prophylactically with sugar-coated quinine sulphate pills.

The whole investigation occupied a year, in the course of which the results were assessed on four occasions. A comparison of the experimental and control groups showed that prophylactic treatment with acriquine and plasmocide brought about a marked diminution in the number of cases of malaria in the former. Treatment of children and others with quinine sulphate was ineffective.

C. A. Hoare.

EDDEY, L. G. **Spray-Killing of Mosquitoes in Houses—a Contribution to Malaria Control on the Gold Coast.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Dec., v. 38, No. 3, 167–88, 1 map & 2 charts. Discussion 188–97 [GORDON, R. M.; JAMES, S. P.; COLLINGWOOD, F. C.; WHITTINGHAM, H.; BLACKLOCK, D. B.; KAUNTZE, W. H.; HACKETT, C. J.; WIGGLESWORTH, V. B.; EDDEY, L. G. (in reply by air letter)].

The harbour and airport at Takoradi in the Gold Coast Colony assumed great strategical importance in 1941. The sudden arrival of large numbers of susceptible European personnel necessitated very vigorous malaria control measures; during the rainy season of 1941 the monthly malaria morbidity rate attained 216·8 per 1,000. Nearby townships constituted the chief danger; it was therefore decided to supplement the usual antilarval and individual prophylactic measures by spray-killing adult mosquitoes in all houses in the central part of Takoradi (population 10,505) and in a group of coastal villages between Takoradi and Sekondi (population 7,162). The paper describes how this work was carried out between November 1942 and November 1943, and the results obtained.

There were some 7,050 rooms to be treated, nearly all of which possessed solid walls, close-fitting doors and louvred or close-batten windows. Two rooms were sprayed at a time; two sprayers worked inside each room and one outside, the latter spraying over the previously closed window and door apertures. After the spraying, the rooms were left closed for 15 minutes; then all dead or stupefied mosquitoes were swept up, and their numbers recorded. The inhabitants were cooperative, appreciating the marked diminution of the mosquito nuisance; locked, and consequently inaccessible, rooms were less than 10 per cent. of the total number during 1943. The onset of the rainy season was followed by a great increase in the numbers of anophelines killed. *A. gambiae*, the chief vector, was much the most prevalent species. *A. funestus* was only occasionally found, and *A. pharoensis* and *A. paludis* very rarely.

In the beginning the insecticidal mixture used was 1 ounce of cresol in one gallon of kerosene, sprayed with a flit-gun type of domestic sprayer. Subsequently, a limited use was made of dry pyrethrum dust, a kerosene extract of pyrethrum, and of pyrethrum aerosol. All methods were effective, but pyrethrum aerosol is the insecticide of choice, and pyrethrum kerosene next best. Limited supplies and high cost made the extended use of dry pyrethrum dust impracticable; the dust has a useful repellent effect. There was but little difference in the over-all cost of spraying with the three liquid preparations, pyrethrum-kerosene, creso-kerosene and pyrethrum aerosol: the cost was slightly over one penny per head per week.

It was not possible to measure with accuracy the degree of malaria control attributable to the spraying. The malaria incidence in one group of Service personnel in 1943 was 42·7 per cent., and in another, 34·2 per cent., of the corresponding incidence in 1942. The general malaria rate of the Services throughout

the Gold Coast was 50 per cent. lower in 1943 than in 1942. These figures suggest that local measures in Takoradi made a noteworthy additional contribution to the protection afforded by anti-malarial measures that were applied throughout the Colony. Further evidence of the protection given by spraying was provided in one village by a much lowered infant infection rate.

In the discussion, Colonel S. P. JAMES expressed gratification that spray-killing adult mosquitoes, a method of malaria control that was advocated by the Malaria Commission of the League of Nations 20 years ago, is being increasingly used. It is to be expected that still better results will be obtained when supplies of the new synthetic insecticide DDT become generally available. Rooms sprayed with DDT remain toxic to mosquitoes for several weeks, and mosquitoes are not repelled by it. It promises to bring nearer the eradication of malaria as the greatest scourge that the world has ever known.

Air Marshall Sir H. WHITTINGHAM considered that the greater reduction in malaria incidence in one group of Service personnel in Takaradi than in another, was indicative of the value of house-screening as a measure of malaria control.

Professor D. B. BLACKLOCK referred to an observation made by the author, that in some of the villages where miles of drains had been cut, there had been an increase of anophelines in the houses. Silting of earth drains with sand, and consequent pool formation—and damage to drains by cattle and by man—create innumerable anopheline breeding places unless the drains receive constant supervision. These surface drains should be replaced by sub-surface drainage. The cost of spraying (a penny per head per week) may seem small but it may well be prohibitive for the family of an African labourer. *Norman White.*

ELLIS, M. M., WESTFALL, B. A. & ELLIS, M. D. **Toxicity of Dichloro-Diphenyl-Trichlorethane (DDT) to Goldfish and Frogs.** *Science.* 1944, Nov. 24, 477.

Goldfish and frogs are more susceptible to DDT than rats, cats and rabbits. Single doses of 63–200 mgm. per kgm. were lethal when dissolved in olive oil and incorporated in food pellets which were swallowed by gold fish weighing 6–10 gm. In this range the mortality was 55 per cent., and was correlated roughly with the size of the dose. Frogs injected with DDT in olive oil were killed in 4–72 hours by single doses of 150 mgm. per kgm.

These findings have a bearing on the use of DDT against mosquito larvae.

Charles Wilcocks.

TALIAFERRO, W. H. & TALIAFERRO, Lucy G. **The Effect of Immunity on the Asexual Reproduction of** *Plasmodium brasilianum.* *J. Infect. Dis.* 1944, July–Aug., v. 75, No. 1, 1–32, 1 pl. & 6 graphs. [25 refs.]

In 1934 the authors [this *Bulletin*, 1935, v. 32, 425] reported upon the behaviour of *Plasmodium brasilianum* in Central American monkeys. It was noted that "the merozoite mean per segmenter varied between 8·5 and 10 and the 3-day periodicity was regular throughout the infection except at the time of the crisis or decrease in parasitaemia, when (1) the asexual cycle sometimes took four or five days instead of three days, (2) the average number of merozoites per segmenter sometimes decreased, and (3) the mean size of the segmenters sometimes decreased," there being a correlation between the size of the segmenters and the number of merozoites. It was concluded that the basic rate of reproduction was constant except at the crisis and that the various aspects of an infection were the result of a differential mortality of parasites during the entire infection, on which was superimposed a temporary retardation of reproduction during some crises. The results presented in the paper under review furnish more exact data and modify the original conclusions to some

extent. They are based on the detailed study of *P. brasilianum* in four *Cebus capucinus* and on a re-examination of 60 similiar infections in 23 white-throated monkeys (*Cebus capucinus*), 6 red spider monkeys (*Ateles geoffroyi*), 9 black spider monkeys (*Ateles dariensis*), 10 howler monkeys (*Alouatta palliata*), six marmosets (*Leontocebus geoffroyi*) and six night monkeys (*Aotus zonalis*).

It was found that significant changes occurred (1) in the synchronism in all marmosets and night monkeys during the entire infection, and in some spider and howler monkeys during the parasite decline ; (2) in the average number of merozoites per segmenter in major and minor broods during the entire infection in the majority of monkeys ; and (3) in the periodicity and morphology of the parasites at the time of the crisis or parasite decline in some monkeys of all species. The extent of these variations from a merozoite number of 8·5 to 10, a 72-hour periodicity and a high degree of synchronism are illustrated in a series of tables and charts. In certain cases, when at the crisis or commencement of decline the 72-hour periodicity is extended to four to five days, a minor brood of parasites may be split off, a fact which may account for changes in type of fever curve during the course of malaria in man. Similar findings were obtained during the acute rise, parasite decline and developed infection of relapses.

The foregoing results are interpreted in terms of immunity. Natural immunity, which functions alone during the acute rise in the infection, is associated with a marked death of parasites and sometimes with a sporadic variation in asexual reproduction. Acquired immunity with continued natural immunity comes into play at the crisis and brings about a heightened death of parasites and, especially during sharp crises, a marked lowering of the rate of reproduction. The lowering of the rate of reproduction at these crises is due to (1) a derangement of the asexual cycle, involving a lack of synchronism and a lengthening of the cycle in some parasites, and (2) a decrease in the number of merozoites in some segmenters as well as the appearance of degenerate crisis forms. These changes are regarded as due to the effect of parasiticidal antibodies, though it is recognized that the changes in the host resulting from the intense antigen-antibody reaction at the time of the crisis may to some extent also be responsible. A series of figures illustrates the various types of segmenters (schizonts) observed in *P. brasilianum* infections, including the evidently abnormal forms which are found at the time of crisis. *C. M. Wenyón.*

BLACKWATER FEVER.

Afonsky, N. P. [**The Treatment of Blackwater Fever by Blood Transfusion.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 72–4. [In Russian.]

The author describes three cases of blackwater fever, one with M.T. parasites in the blood, another with a history of malaria in the past, and the third who had never suffered from malaria or taken quinine. All three patients who manifested severe symptoms, showed dramatic improvement after blood transfusion (200 cc.) and were discharged as cured. It is concluded that in blackwater fever blood transfusion is indicated in all cases and should not be delayed until severe symptoms make their appearance. This form of treatment is regarded as fundamental, and not merely supplementary. *C. A. Hoare.*

TRYPANOSOMIASIS.

STÉFANOPOULO, G. & ÉTÉVÉ, J. Méningo-encéphalo-myélite de la souris blanche due à une souche "neurotrope" de *Tr. gambiense.* [**Meningo-Encephalo-Myelitis of the White Mouse due to a "Neurotropic" Strain of** *Trypanosoma gambiense.*] *Bull. Soc. Path. Exot.* 1943, Jan. 13 & Feb. 10, v. 36, Nos. 1–2, 43–5, 6 figs. on 3 pls.

The authors have examined white mice, infected with a strain of *Trypanosoma gambiense* that had been found by ROUBAUD and PREVOST [this *Bulletin*, 1942, v. 39, 234] to have neurotropic properties for mice. These animals have been generally considered to get a blood infection only. Of 19 infected mice 9 showed symptoms of paralysis, and of these, 5 had been inoculated intraperitoneally and 4 intracerebrally. The former showed paralytic symptoms in different animals 68 to 189 days after inoculation, the latter after 41 to 228 days. Three of the mice died spontaneously after 28, 41 and 44 days, and the other six were killed from 1 to 59 days after paralysis appeared. In mice which did not develop paralysis the infection had a shorter course and trypanosomes were more constantly present in the blood.

At autopsy the lymph glands were found much enlarged but the spleen and liver showed little macroscopic change. The brain was hyperaemic and in some cases oedematous. The histological lesions of the central nervous system are described; they resembled those recorded by PLIMMER [*Proc. Roy. Soc.*, 1907, Ser. B, v. 79, 95] in rats (which become paralysed) and by other workers. Perivascular infiltration by lymphocytes and plasma cells and meningitis are present but the authors found no changes in the choroid plexus or ependyma nor did they see any morular cells of MOTT [*Rep. Sleeping Sickness Comm. Roy. Soc.*, 1906, No. 7, 15]. The kidneys and liver also showed lymphocytic infiltration similar to that described by PETTIT [*Sleeping Sickness Bulletin*, 1911, v. 3, 264] who called it lymphoid transformation of the liver.

In discussion ROUBAUD suggested that the mouse may perhaps serve to test the greater or less tendency of different human strains of trypanosomes to infect the nerve centres. *J. F. Corson.*

BROWNING, C. H., BROWNING, P. & ROBB, J. V. M. **A Phenanthridinium Compound of Morgan and Walls as a Chemotherapeutic Agent in Experimental Infections with** *T. congolense.* *J. Path. & Bact.* 1940, v. 50, 371–2.

It was found by BROWNING and his co-workers [this *Bulletin*, 1938, v. 35, 344] that one of a series of phenanthridinium compounds, 7-amino-9 (*p*-aminophenyl)-10 methylphenanthridinium chloride, possessed curative action in mice infected with *Trypanosoma congolense.* Further work has shown that the infection may be cured with 1/60-1/100 of the maximum tolerated dose, given subcutaneously. On the other hand, *T. brucei* infection was cured only by a dose near the maximum. Prophylactic action against *T. congolense* was found to be slight.

As regards toxicity, a dose of 0·005 gm. per kgm. intravenously as a 1 : 400 solution caused no illness; 0·013 gm. might be fatal at once, or this dose or 0·01 gm. might cause illness followed by rapid recovery and no later ill effects.

J. F. Corson.

BROWNING, C. H. & CALVER, K. M. **The Effect of the Stage of Infection on the Chemotherapeutic Response of** *T. congolense* **and on the Immunity following Cure.** *J. Path. & Bact.* 1943, v. 55, No. 3, 393–4.

Two strains of *Trypanosoma congolense* were used in a study of the biological aspects of cure of the infection in mice by 7-amino-9 (*p*-aminophenyl)-10 methylphenanthridinium chloride [see BROWNING, BROWNING and ROBB above, p. 258]. One of the strains, no. I, usually caused relapsing infections, while in the other, no. II, which caused a more severe illness, numerous trypanosomes persisted in the blood until death occurred, after a few days to several weeks. Treatment was more effective at the acme stage [when trypanosomes are abundant] than earlier, and this suggests that an immunity reaction plays a significant part in the cure.

Infections produced by inoculation from a chronic infection of either strain required much larger doses for cure than infections produced by inoculations of the same strains at the acme stage. If, in animals inoculated with "acme" trypanosomes, treatment is delayed until the infection has become chronic, cure may be difficult.

The immunity produced after cure with the drug was much more "solid" in strain I than in strain II infections. There was no immunity, however, to the trypanosomes of chronic infection, and there was no cross immunity between the strains. When a chronic strain was passed at the acme stage through a series of fresh mice it sometimes regained its acme character, as shown by the immunity test, by the 5th passage, but, on the other hand, the chronic character might persist for 7–11 passages or more.

With this drug the ultimate chance of cure in a relapse appeared to be as good as in the initial infection; occasionally, evidence of drug-resistance was obtained.

The authors suggest that, under field conditions, therapeutic results may depend on the strain of *T. congolense*, the stage of infection and other factors, and that failure to cure relapses does not necessarily imply drug-resistance. The part played by cyclical development in the tsetse fly, is, of course, not indicated by these experiments. *J. F. Corson.*

CARMICHAEL, J. & BELL, F. R. **A Study of the Therapeutic Action of the Phenanthridinium Compound 897 against** *Trypanosoma congolense* **Infection in Cattle.** *J. Comp. Path. & Therap.* 1944, Jan., v. 54, No. 1, 49–52.

The new drug S.897, 7-amino-9 (*p*-aminophenyl)-10 methylphenanthridinium chloride, having been shown by BROWNING *et al.* [see above] to cure *T. congolense* infection in mice, the authors tried it in experimental infections of cattle; two laboratory strains of *T. congolense* were used and the cattle were presumably infected by inoculation. The toxicity of the drug was first tested in eight cattle; the highest non-toxic dose, intravenously, was 3 mgm. per kgm. body weight which, owing to the low solubility of the drug, required a volume of solution that was hardly practicable for general use. The drug appeared to produce no change in the blood of the animals.

Six cattle were infected with *T. congolense* and four were given a dose of 2 mgm. per kgm. when they were in the chronic stage of the disease; all were cured, *i.e.* they became well, their blood showed no trypanosomes on daily examination for four months, and subinoculation into susceptible cattle proved negative.

In a second experiment a herd of 40 infected cattle was divided into five groups of eight animals and treated with a dose of 2 mgm. per kgm. by various routes; the results are shown in Table III:—

TABLE III.

Route of Administration	Result
1. Intravenous	3 cured, 4 relapsed, 1 death intercurrent infection.
2. Subcutaneous	2 cured, 5 relapsed, 1 death intercurrent.
3. Intramuscular	1 cured, 7 relapsed.
*4. Intravenous and subcutaneous ...	1 cured, 7 relapsed.
*5. Intravenous and intramuscular ...	4 cured, 4 relapsed.

*Half the total dose was given by each route.

The initial treatment cured 11 animals, 27 relapsed, and 2 died from intercurrent conditions. The relapsed cases were re-treated by an intravenous injection of 2 mgm. per kgm. given 44 days after the first treatment; 22 were cured. All the relapses had occurred 14–29 days after treatment. Five (all infected with the same strain) which again relapsed were similarly re-treated after another 49 days but again relapsed, and a fourth treatment was also ineffectual.

Intramuscular injections caused stiffness and lameness.

The authors consider the intravenous, or the intravenous plus the intramuscular, route to be best. An experiment showed that a dose of 2 mgm. per kgm. protected up to 48 hours against a very heavy inoculation of trypanosomes.

J. F. Corson.

CARMICHAEL, J. & BELL, F. R. **The Use of a New Phenanthridinium Compound 1553 in the Treatment of *Trypanosoma congolense* Infection in Cattle.** Reprinted from *Vet. Record.* 1944, Dec. 16, 2 pp.

A new phenanthridinium compound (1553)—2 : 7-diamino-10 methylphenanthridinium bromide—was stated by BROWNING (private communication) from whom the authors received it, to be more active than S.897 [above] and to cause less induration at the site of injection. A 4 per cent. solution can be obtained easily in hot water and the drug remains in solution on cooling; the solution has a port-wine colour.

The authors tested the drug on humped cattle (zebu) infected with *Trypanosoma congolense* by subcutaneous inoculation, three recently isolated virulent strains being used. In the first experiment, a dose of 2 mgm. per kgm. was given as a 2 per cent. solution when trypanosomes were numerous in the blood; the results are shown in Table I :—

TABLE I.

No. of zebus	Route of administration	Cures	Relapses
4	Intramuscular	4	—
12	Subcutaneous	8	4
4	Intravenous	4	—

The trypanosomes disappeared from the blood within 24–48 hours. The four relapses were again treated with the same dose subcutaneously between the 13th and 24th days after the first injection and all were cured, the test of cure being: the blood was free from trypanosomes on daily examination for four

months ; the blood returned to normal ; the bodily condition improved ; and inoculation of mice was negative. Intramuscular injections caused painful swelling and lameness which persisted for some weeks, but there was no sloughing ; subcutaneous injections, however, caused very little reaction.

In the second experiment the drug was given subcutaneously (with various slight modifications) to 19 zebus with chronic *T. congolense* infection ; the details and results are shown in Table II :—

TABLE II.

Dose : mgm. per kgm.	Percentage Solution 1553	
	2 per cent.	1 per cent.
1·0	4 4C	4 4C
1·5	4 4C	4 4C
2·0	— —	3 3C

C=Cured.

Only one animal showed a local reaction ; it had received a 1 per cent. solution and massage was not done.

The experiment shows that the compound has very high curative properties for *T. congolense* infections, all the 39 cattle being cured. The toxicity of the drug was not investigated but the authors believe that it is low.

J. F. Corson.

SEAGER, L. D. **Transmission of** *Trypanosoma equiperdum* **to the Duck.** *Science.* 1944, Nov. 10, 428.

The author injected *Trypanosoma equiperdum* in doses of 500 millions per kgm. of body weight intravenously into ducklings one week old. Four groups [number not stated] showed no trypanosomes in the blood on examination during 8–12 days ; two died, on the 14th and 15th days respectively, and the latter had numerous trypanosomes in its blood ; mice, subinoculated from it, died of trypanosomiasis on the 4th day after inoculation. Ten other week-old ducklings were also inoculated intravenously and observed for 18 days ; two showed trypanosomes in the blood on the 10th day and died of trypanosomiasis on the 12th and 14th days respectively. The blood of the other eight ducklings showed no trypanosomes, but when it was inoculated intraperitoneally into mice, it produced fatal infections in all.

The author states that " the implications of these findings as to possible avian reservoirs of similar mammalian parasites is obvious." [Several workers have transmitted human and other mammalian pathogenic trypanosomes to various species of birds—fowls, geese, ducks, guineafowl, francolins—see *Sleeping Sickness Bulletin*, 1909, v. 1, No. 5, 201 ; 1912, v. 4, No. 39, 277 ; this *Bulletin*, 1931, v. 28, 921 ; 1932, v. 29, 837 ; 1933, v. 30, 454 ; 1935, v. 32, 710. Avian blood has been found in nature in tsetse flies.] *J. F. Corson.*

LEISHMANIASIS.

RAMAN, T. K. **Kala-Azar in Non-Endemic Areas.** *J. Indian Med. Ass.* 1944, Oct., v. 14, No. 1, pp. 8 & 7.

The author reports that during 1933–1942 twelve cases of kala azar were admitted to the King George Hospital, Vizagapatam, which is not an endemic centre for this disease. Ten of the cases had their origin in Madras or Calcutta but in two the patients had never left Vizagapatam or its neighbourhood. It was difficult to account for infection in these two cases. The suggestion is made that it was contracted orally. The aldehyde test was carried out in 200 unselected cases in Guntur, where no cases of kala azar had been met with. It was strongly positive in 4 per cent. of these, moderately positive in 7 per cent. and slightly positive in 8·5 per cent. In none of these cases was it possible to establish a diagnosis of kala azar, though every test was applied. Three similar cases with strongly positive aldehyde test and enlarged spleen were seen in Vizagapatam. No leishmania could be found by spleen puncture. *C. M. Wenyon.*

WERTHEIMER, E. & STEIN, L. **The Cold-Susceptible Globulin Fraction of Pathologic Sera.** *J. Lab. & Clin. Med.* 1944, Oct., v. 29, No. 10, 1082–9.

In an earlier paper [see this *Bulletin*, 1942, Vol. 39, p. 747] the authors showed that the serum from cases of kala azar in human beings and dogs contained a protein fraction which came out of solution as a flocculent precipitate when the serum was kept at a temperature of 7–11°C. It was named the Cold Fraction (C.F.) and was found to be related to euglobulin. In the present paper an account is given of further studies on this C.F. It has been found that for complete separation an exposure to cold for three days is necessary. There are five degrees or types of separation, as follows: turbidity, light precipitate, flocculent precipitate, precipitate capable of estimation by quantitative methods and a different precipitate found as a layer on the surface. In five cases of kala azar in human beings and in three cases in dogs the C.F. was present in varying degree, as shown in tables. It was noted that if, as a result of treatment, clinical cure was obtained (with a rise in the albumin of the serum, a fall in the globulin, particularly the euglobulin, and a decrease in the intensity of other abnormal serological reactions), the C.F. nevertheless persisted for long periods. The question arises as to whether cure can be regarded as having taken place in such circumstances. Further observations on a more extended scale will be needed to supply the answer. It was shown in cases of kala azar in dogs that the abnormal globulin, euglobulin, C.F., and other fractions persisted in spite of chronic protein hunger and extensive loss of blood. The C.F. has been shown to be present in cases of endocarditis lenta, while in lipoid nephroses, the final phase of chronic uraemia, and in cirrhotic changes of the liver, a C.F. of a peculiar nature occurs in the serum. It is stated that in 13 cases of *Leishmania cutis* (Jericho rose) C.F. of grade 2 was present in one case. [It is evident that the term *Leishmania cutis* is intended for leishmaniasis cutis and not for a new species of *Leishmania*]. *C. M. Wenyon.*

GOODWIN, L. G. **The Chemotherapy of Experimental Leishmaniasis. I. The Spleen as an Index of Infection in the Syrian Hamster.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Nov., v. 38, No. 2, 151–60, 2 figs. [20 refs.]

With the object of working out a reliable test for therapeutic activity of drugs against *Leishmania donovani* the author has investigated the possible

errors associated with the method adopted by ADLER and TSCHERNOMORETZ [this *Bulletin*, 1940, v. 37, 775 ; 1942, v. 39, 173 & 748] which consisted in making stained smears from portions of spleen removed from infected hamsters before and after treatment and counting the number of parasites per hundred cell nuclei. The possible sources of error are: the counting of an inadequate number of parasites and nuclei, uneven distribution of parasites in the spleen, sporadic changes in the intensity of infection, the drug may not act equally on all parts of the spleen. These various sources of error are carefully investigated by the author. It was determined that in spleens in which there occurred 50 or more parasites per 100 cell nuclei a fair estimate of the degree of infection can be obtained by counting the parasites against 250–500 nuclei. For infections of less than 10 parasites per 100 nuclei, 500 to 1,000 nuclei must be counted. It was also found that there was a fairly even distribution of parasites throughout an infected spleen, while untreated animals show a steady increase of infection which may be very rapid after spleen biopsy. Single subcutaneous doses of organic antimonials have been shown to have a measurable effect upon parasite counts in the spleen, an effect which is uniform throughout the organ. The films for counting purposes were made by dabbing on slides the cut surfaces of portions of spleen removed by biopsy. They were stained by Giemsa stain. The author concludes that his observations form a sound basis upon which therapeutic potency tests may be designed. *C. M. Wenyon.*

PATEL, J. C. **Six Cases of Kala-Azar in Bombay. Sodium Antimony V Gluconate in its Treatment.** *Indian Physician.* 1944, Nov., v. 3, No. 11, 319–27. [26 refs.]

In this paper the author describes the treatment of six cases of kala azar in Bombay. All were imported from the United Provinces, Bihar or Bengal. Three of the patients were adults and three children 8, 10 and 14 years of age respectively. Diagnosis was established by the finding of leishmania in smears or leptomonads in cultures from sternal puncture material. All cases were treated with sodium antimony V gluconate (stibatin of Glaxo Laboratories). It was found that the adults would tolerate 10 daily injections of 20 cc. of the solution, which is of such strength that 1 cc. contains 20 mgm. of metallic antimony. Accordingly, after trials in the first case treated, this dosage was adopted for the other two adults, one receiving the 10 doses intravenously and the other intramuscularly. As regards the three children, the youngest had intravenous injections of 12 cc. for 10 days (120 cc.), the one 10 years of age 15 cc. intravenously for 10 days (150 cc.) and the eldest 1 dose of 5 cc. and nine doses of 6 cc. intramuscularly (59 cc.) during ten days.

In no case were any toxic symptoms noted, and cessation of symptoms and improvement in general health occurred in all. One child, 10 years of age, died of tuberculous meningitis four months after treatment. There was no indication of kala azar at the time of death. Four of the other five patients, followed for six or more months, are regarded as permanently cured. One is still under observation. It is noted that in one case a positive culture was obtained from sternal puncture material after the course of treatment has been completed. Six months later, culture was negative and a permanent cure registered.

The author concludes that sodium antimony V gluconate is the drug of choice in the treatment of kala azar, as it has so many advantages over neostibosan and urea stibamine. He considers that it should be given extensive trials in endemic areas. A more concentrated solution in which 1 cc. contained 50 mgm. of the drug in place of the usual 20 mgm., had been tried. It seemed that the advantages of a reduction in bulk of fluid to be injected was probably counterbalanced by the greater amount of antimony required. *C. M. Wenyon.*

FULLER, A. T. **A Colour Reaction for Aromatic Amidines.** [Correspondence.] *Nature.* 1944, Dec. 16, 773.

DEVINE [this *Bulletin*, 1944, v. 41, 930] described a method for the colorimetric determination of stilbamidine based on the observation of EKELY & RONZIO (*Jl. Amer. Chem. Soc.*, 1935, v. 57, 1353), that certain aromatic diamidines, heated with glyoxal in alkaline solution, yield coloured derivatives. In the present independent investigation the method has been modified and made more sensitive and reliable, by heating in a borate buffer at *p*H 9. It has proved suitable for the estimation of aromatic amidines at a dilution of 1 in 100,000. The buffer was prepared from 4 gm. boric acid neutralized in hot solution with caustic soda to *p*H 9, and diluted to 100 cc. The glyoxal reagent was used as the sodium bisulphite in 0·5 per cent. aqueous solution. When carrying out an estimation, a few cc. of the amidine solution, roughly neutralized, were mixed with about 1 cc. of each of the reagents, and the mixture maintained near the boiling point for a few minutes, or left on the water bath for 10 minutes, when a pink or magenta colour was produced. The best development of colour was obtained with approximately two molecules of the reagents to one of amidine. The reaction, which is specific for an unsubstituted aromatic amidine group, is inhibited by excess of glyoxal. The reaction does not take place with compounds in which one or two methyl groups are attached to the nitrogen of the amidine group, nor with guanidines, biguanidines, amines or aliphatic amidines. In some cases the reaction products with aromatic amidines showed fluorescence in ultra violet light at a dilution of 1 in 100 millions. *J. D. Fulton.*

SEN GUPTA, P. C. **Phenamidine in the Treatment of Kala-Azar.** [Correspondence.] *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 508.

COSTA, O. G. **Mutilating Form of American Leishmaniasis.** *Arch. Dermat. & Syph.* 1944, Nov., v. 50, No. 5, 328, 2 figs.

Report of a case.

FEVERS OF THE TYPHUS GROUP.

VAN ROOYEN, C. E., BOWIE, J. H. & KRIKORIAN, K. S. **Typhus Research in Egypt, Palestine, Iraq and Iran.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Nov., v. 38, No. 2, 133–49. [18 refs.]

This paper is a shorter and much more attractive version of the one reviewed in this *Bulletin*, 1945, v. 42, 194. It is welcome because the previous article is not likely to be accessible to many workers on the subject.

After extensive trials of the Weil-Felix and rickettsia-agglutination tests the authors make the following statement—"On the 4th or 5th day the Weil-Felix titre is invariably below the normal titre of 1–100 ; . . . on the 6th or 7th day a low titre *OX19* and similar positive rickettsial agglutination occasionally may be observed to a serial dilution of 1–200 . . . . On the 8th and 9th day the two reactions are usually positive to a titre of 1–400. From the 10th to 14th day both reactions become strongly positive and many vary from 1–800 to 1–6,400 . . . . From the 14th to 21st day very high titre *OX19* and rickettsial-agglutination is invariably present in severe epidemic typhus." The rickettsia reaction is held to be superior to the Weil-Felix in its ability to differentiate between epidemic and murine typhus, but, on the other hand, the antigen is

very costly and the flocculation is difficult to observe when the titre of the reaction is low, so that the best results are obtained between the 10th and 15th days.

A table in the paper gives the various titres observed in 119 cases, all but three of which were diagnosed as murine or epidemic on the strength of the higher-titre agglutination to one or other of the two types of rickettsiae. In most of the cases the differences in titre were great, but among the last 23 cases diagnosed as murine there were seven in which the " murine titre " was only twice as high, or less than twice as high, as the " epidemic titre."

The following extract from the table shows the results obtained in one special group of six consecutive cases which occurred within a period of seven days in July 1943 at Quassassim.

Serial number	*Proteus OX19* titre	Epidemic rickettsia titre	Murine rickettsia titre	Diagnosis
94	500	1,600	400	Epidemic
95	200	100	500	Murine
96	3,200	800	1,600	Murine
97	300	300	800	Murine
98	200	500	800	Murine
99	400	400	500	Murine

[This group is exceptional, but it suggests the possibility that some infections may be caused by organisms which are intermediate in their agglutinin-producing properties between the frankly epidemic and the frankly murine types.] *John W. D. Megaw.*

HERRERA, J. R. Informe sobre tifo exantemático ocurrido en la ciudad de Guatemala durante el mes de abril de 1944. [**Report on an Outbreak of Typhus Fever in the City of Guatemala in April, 1944.**] *Bol. Oficina Sanitaria Panamericana.* 1944, July, v. 23, No. 7, 603–7, 1 fig. English summary.

This outbreak occurred in The Home for the Insane of Guatemala; its chief interest lies in the fact that about 88 cases with 25 deaths had occurred during the month preceding the date on which the existence of a communicable disease in the institution was notified to the health authorities. Control measures on orthodox lines were carried out with energy, and in less than a month the epidemic came to an end.

During the month of April, after the notification of the disease, there were 198 proved cases with 63 deaths in the home, and 30 cases were detected elsewhere in the City. *John W. D. Megaw.*

PATIÑO-CAMARGO, L. Tifo exantemático en Colombia. [**Typhus in Colombia.**] *Bol. Oficina Sanitaria Panamericana.* 1944, Aug., v. 23, No. 8, 675–6. English summary.

" Of 1,319 cases of typhus reported in Colombia, 752 were reported from the hospitals of Bogotá (303 women, 482 men; 51 deaths, mortality 6·64%). There were cases in 34 municipalities of Antioquia, 6 municipalities of Boyacá, 2 of Cauca, 7 of Caldas, 18 of Cundinamarca (including Bogotá), 9 of Nariño, 2 of Santander, and 1 of Tolima. Verification was made by isolation of the virus from blood of patients inoculated into guinea pigs, through finding of

Rickettsia, and by agglutination with *Proteus*. No spotted fever was verified during the year 1943." [Elsewhere the figures are given as: women 292, men 460. This total appears to be correct.—*Ed.*]

AVTSYN, A. P. [**The Pathology of Exanthematic Typhus.**] *Klinicheskaia Meditsina.* Moscow. 1944, v. 22, No. 4, 44–52. [17 refs.] [In Russian.]

When mice are inoculated intranasally with suspensions of rickettsia a specific bronchopneumonia is produced, which passes through the following stages:—(1) after one hour: swelling of alveolar epithelium, some desquamation, with single rickettsiae in the cast-off cells. (2) 12–18 hours: vascular reaction, diffuse hyperaemia of lungs, rickettsiae present in the alveolar epithelium. (3) 24–48 hours: formation of foci of bronchopneumonia. (4) 60–90 hours: extensive consolidation, necrotic foci surrounded by haemorrhagic areas. Many rickettsiae present, in bronchial and vascular endothelium, and also in giant cells; not seen in lymph nodes nor in smooth muscle fibres of bronchi and blood vessels. In the early stages bodies resembling droplets were seen in the bronchial and alveolar epithelium, having the same staining reactions as rickettsiae. These can, however, be scarcely considered as initial bodies, as they were also seen in the liver, where rickettsiae were not found, and also in the bronchial epithelium of mice with streptococcal pneumonia. It is suggested that they represent a cellular reaction to the presence of the parasite. The effect of rickettsial endotoxin was observed by injecting mice intranasally with a massive dose of virulent lung suspension. Death occurred in 24 hours, with hyperaemia of the lungs and haemorrhages. *D. J. Bauer.*

WILCKENS, H. Zur Klinik des Fleckfiebers. [**Clinical Aspects of Typhus Fever.**] *Med. Klin.* 1943, Oct. 1, v. 39, No. 39/40, 671–4. [14 refs.]

These notes are based on the observation of 315 cases, mostly very severe, of typhus fever seen in the months of January, February and March, 1943, in a Field Hospital in the "Middle East." There were 40 deaths.

The patients were inclined to be somnolent by day and excited by night. When the wards were brightly lighted at night this inversion of the "day and night rhythm" became less pronounced. More than two-thirds of the deaths occurred before the end of the febrile period. Twelve patients who had been inoculated suffered from exceptionally mild attacks, but several patients whose illness began before the third dose of vaccine was given had attacks of average severity. A high-intermittent type of fever curve was usual in cases with pneumonia or septic complications. An "after fever" lasting 1–2 days was often seen shortly after defervescence. The author believed that a rickettsial endotoxin played a more important part in the early stages of the illness than the arterial lesions; in one patient who died on the 5th day very few typhus nodules were found in the brain. An unusual complication was diphtheria, which occurred in 14 cases, and was regarded as the cause of death of five patients; in septic complications there seemed to be no failure in the development of immunity to the secondary infection; healing was surprisingly satisfactory.

In a considerable number of cases a fine powdery desquamation was seen on the face for some time after defervescence, though the typhus rash had not been detected on the face in any of the patients. There were no cases of gangrene. Pressure sores were rare and when they did occur they yielded readily to treatment. The lunulae of the nails were observed to assume the same colour as the rest of the nails early in the course of the fever. The urine contained cylindrical casts and small quantities of albumin in all cases.

No great claims are made for any kind of drug treatment. Calcium gluconate and atebrin were tried at the beginning of the epidemic, but the author formed

the opinion that luminal gave better results. He gave this drug in doses of 0·03 gramme five times daily and also a single dose of 0·2 gramme every evening. Strophanthin was given intravenously every two days and "sympatol" was injected subcutaneously every two hours.

Convalescence was very slow, a period of at least 4–6 months was found to be essential. *John W. D. Megaw.*

LAURE, G. Remarques cliniques et thérapeutiques sur les gangrènes du typhus. [**Clinical and Therapeutic Observations on Gangrene in Typhus Fever.**] *Bull. Inst. Hyg. Maroc.* 1943, v. 3, 59–86, 2 pls.

The author saw 120 cases of gangrene among 2,014 typhus patients in French Morocco during the year 1942. He classifies the disease in two groups, one of which, the common type, is called "distal"; the other, in which a considerable part of one or both limbs is affected, is called "global." In both types the gangrene is usually dry, being caused by a purely arterial lesion, but in some cases the veins also are affected and there is a combination of dry and moist gangrene. The global type tends to occur early in the course of the fever, the distal type appears late in the illness, often during convalescence.

Few females were attacked, no case was seen among Jewish patients, and among 50 European patients there were only three cases. In nearly all the cases the disease was restricted to the lower extremities.

Distal gangrene, which usually affects both limbs, is described as being of three degrees of severity: (*a*) the least severe, appearing most commonly in early convalescence. The first symptom is pain in the tips of the toes, which later become pale and cold and soon take on a livid hue. By the end of 4–6 days a superficial patch of dry gangrene appears on the distal and plantar aspect of one or more of the toes. The great toe is affected more often than the others. Spontaneous cure with the separation of a small slough is usual. (*b*) The average type sometimes occurs as an extension of type (*a*), sometimes the greater part of the toes is affected from the beginning; the gangrene may extend as far as the metatarso-phalangeal joint. In all cases the deeper tissues are involved. The line of demarcation becomes sharp 10–15 days after the onset and a natural amputation soon follows. (*c*) The severe type, which may be an extension of type (*b*) or may set in with rapid involvement of the whole or greater part of the foot.

Global gangrene is usually bilateral. The onset tends to be sudden; half or two-thirds of one or both legs becomes cold, painful, and cyanosed, almost simultaneously. The popliteal pulse is imperceptible and the femoral pulse is feeble. Mummification is apparent within 4–5 days. Occasionally the condition is a gradual extension of the severest form of distal gangrene.

Moist gangrene is usually a complication of the dry form, it usually starts above the line of demarcation, but occasionally the gangrene is moist from the outset.

The treatment specially recommended is blocking of the lumbar sympathetic ganglion by infiltration with 10–20 cc. of 1–200 solution of novocain, without adrenaline. The needle is inserted at a point four fingers' breadth from the tip of the spinous process of the 2nd lumbar vertebra [presumably measured on a horizontal line] and is inclined at an angle of 60° till it touches the vertebral column, when the needle is brought to a vertical position and is made to follow the plane of the bone till the end of its travel. [These instructions cannot be regarded as a complete guide to a novice.] After a successful infiltration the limb immediately feels warm, and if the treatment is started early the pain disappears or is greatly relieved after two injections. After four or five injections given daily the limb becomes warm and the slough becomes absorbed. It is

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Rickettsia, and by agglutination with *Proteus*. No spotted fever was verified during the year 1943." [Elsewhere the figures are given as: women 292, men 460. This total appears to be correct.—*Ed.*]

AVTSYN, A. P. [**The Pathology of Exanthematic Typhus.**] *Klinicheskaia Meditsina.* Moscow. 1944, v. 22, No. 4, 44–52. [17 refs.] [In Russian.]

When mice are inoculated intranasally with suspensions of rickettsia a specific bronchopneumonia is produced, which passes through the following stages:—(1) after one hour: swelling of alveolar epithelium, some desquamation, with single rickettsiae in the cast-off cells. (2) 12–18 hours: vascular reaction, diffuse hyperaemia of lungs, rickettsiae present in the alveolar epithelium. (3) 24–48 hours: formation of foci of bronchopneumonia. (4) 60–90 hours: extensive consolidation, necrotic foci surrounded by haemorrhagic areas. Many rickettsiae present, in bronchial and vascular endothelium, and also in giant cells; not seen in lymph nodes nor in smooth muscle fibres of bronchi and blood vessels. In the early stages bodies resembling droplets were seen in the bronchial and alveolar epithelium, having the same staining reactions as rickettsiae. These can, however, be scarcely considered as initial bodies, as they were also seen in the liver, where rickettsiae were not found, and also in the bronchial epithelium of mice with streptococcal pneumonia. It is suggested that they represent a cellular reaction to the presence of the parasite. The effect of rickettsial endotoxin was observed by injecting mice intranasally with a massive dose of virulent lung suspension. Death occurred in 24 hours, with hyperaemia of the lungs and haemorrhages. *D. J. Bauer.*

WILCKENS, H. Zur Klinik des Fleckfiebers. [**Clinical Aspects of Typhus Fever.**] *Med. Klin.* 1943, Oct. 1, v. 39, No. 39/40, 671–4. [14 refs.]

These notes are based on the observation of 315 cases, mostly very severe, of typhus fever seen in the months of January, February and March, 1943, in a Field Hospital in the "Middle East." There were 40 deaths.

The patients were inclined to be somnolent by day and excited by night. When the wards were brightly lighted at night this inversion of the "day and night rhythm" became less pronounced. More than two-thirds of the deaths occurred before the end of the febrile period. Twelve patients who had been inoculated suffered from exceptionally mild attacks, but several patients whose illness began before the third dose of vaccine was given had attacks of average severity. A high-intermittent type of fever curve was usual in cases with pneumonia or septic complications. An "after fever" lasting 1–2 days was often seen shortly after defervescence. The author believed that a rickettsial endotoxin played a more important part in the early stages of the illness than the arterial lesions; in one patient who died on the 5th day very few typhus nodules were found in the brain. An unusual complication was diphtheria, which occurred in 14 cases, and was regarded as the cause of death of five patients; in septic complications there seemed to be no failure in the development of immunity to the secondary infection; healing was surprisingly satisfactory.

In a considerable number of cases a fine powdery desquamation was seen on the face for some time after defervescence, though the typhus rash had not been detected on the face in any of the patients. There were no cases of gangrene. Pressure sores were rare and when they did occur they yielded readily to treatment. The lunulae of the nails were observed to assume the same colour as the rest of the nails early in the course of the fever. The urine contained cylindrical casts and small quantities of albumin in all cases.

No great claims are made for any kind of drug treatment. Calcium gluconate and atebrin were tried at the beginning of the epidemic, but the author formed

the opinion that luminal gave better results. He gave this drug in doses of 0·03 gramme five times daily and also a single dose of 0·2 gramme every evening. Strophanthin was given intravenously every two days and "sympatol" was injected subcutaneously every two hours.

Convalescence was very slow, a period of at least 4–6 months was found to be essential. *John W. D. Megaw.*

LAURE, G. Remarques cliniques et thérapeutiques sur les gangrènes du typhus. [**Clinical and Therapeutic Observations on Gangrene in Typhus Fever.**] *Bull. Inst. Hyg. Maroc.* 1943, v. 3, 59–86, 2 pls.

The author saw 120 cases of gangrene among 2,014 typhus patients in French Morocco during the year 1942. He classifies the disease in two groups, one of which, the common type, is called "distal"; the other, in which a considerable part of one or both limbs is affected, is called "global." In both types the gangrene is usually dry, being caused by a purely arterial lesion, but in some cases the veins also are affected and there is a combination of dry and moist gangrene. The global type tends to occur early in the course of the fever, the distal type appears late in the illness, often during convalescence.

Few females were attacked, no case was seen among Jewish patients, and among 50 European patients there were only three cases. In nearly all the cases the disease was restricted to the lower extremities.

Distal gangrene, which usually affects both limbs, is described as being of three degrees of severity: (*a*) the least severe, appearing most commonly in early convalescence. The first symptom is pain in the tips of the toes, which later become pale and cold and soon take on a livid hue. By the end of 4–6 days a superficial patch of dry gangrene appears on the distal and plantar aspect of one or more of the toes. The great toe is affected more often than the others. Spontaneous cure with the separation of a small slough is usual. (*b*) The average type sometimes occurs as an extension of type (*a*), sometimes the greater part of the toes is affected from the beginning; the gangrene may extend as far as the metatarso-phalangeal joint. In all cases the deeper tissues are involved. The line of demarcation becomes sharp 10–15 days after the onset and a natural amputation soon follows. (*c*) The severe type, which may be an extension of type (*b*) or may set in with rapid involvement of the whole or greater part of the foot.

Global gangrene is usually bilateral. The onset tends to be sudden; half or two-thirds of one or both legs becomes cold, painful, and cyanosed, almost simultaneously. The popliteal pulse is imperceptible and the femoral pulse is feeble. Mummification is apparent within 4–5 days. Occasionally the condition is a gradual extension of the severest form of distal gangrene.

Moist gangrene is usually a complication of the dry form, it usually starts above the line of demarcation, but occasionally the gangrene is moist from the outset.

The treatment specially recommended is blocking of the lumbar sympathetic ganglion by infiltration with 10–20 cc. of 1–200 solution of novocain, without adrenaline. The needle is inserted at a point four fingers' breadth from the tip of the spinous process of the 2nd lumbar vertebra [presumably measured on a horizontal line] and is inclined at an angle of 60° till it touches the vertebral column, when the needle is brought to a vertical position and is made to follow the plane of the bone till the end of its travel. [These instructions cannot be regarded as a complete guide to a novice.] After a successful infiltration the limb immediately feels warm, and if the treatment is started early the pain disappears or is greatly relieved after two injections. After four or five injections given daily the limb becomes warm and the slough becomes absorbed. It is

claimed that early treatment arrests the course of the disease, and that even at a later stage the relief of pain enables the surgeon to continue to "temporize" and wait for a natural termination of the disease, with its resultant economy in the loss of tissue. But the attitude of temporizing and economizing must not be adhered to in cases with secondary infections; in these the result may be a greater risk to life, and if recovery occurs the final loss of tissue may be much greater.

John W. D. Megaw.

LEMAIRE, G. Contribution à l'étude des effets du vaccin de G. BLANC. Vaccination massive d'un foyer épidémique. Expérience de la Casbah. Difficultés d'interprétation des statistiques relatives aux milieux indigènes. [**A Contribution to the Study of the Effects of Blanc's Vaccine.**] *Bull. Soc. Path. Exot.* 1943, July 7, v. 36, Nos. 7–8, 202–7.

The new type of Blanc's living vaccine has the great advantage of keeping for an indefinite period when stocked in dry form *in vacuo*.

About 35,000 persons, constituting 70 per cent. of the population of the quarter, were inoculated in the Casban section of Algiers within seven days in February 1942, during an epidemic.

Carefully controlled observation of the results was made, starting 37 days after the completion of the inoculation so as to allow for the maximum incubation period of 27 days (for inoculated murine typhus) and an extra margin of 10 days for any possible extension of this period.

From March 25th to August 1st there were 121 cases with four deaths among 35,000 inoculated persons, and 422 cases with 73 deaths among 15,000 non-inoculated persons.

The case incidence was, therefore, 8 times higher among the unprotected than among the protected, and the case-fatality rate was five times higher in the former than in the latter group.

BLANC is quoted as stating that about 40 per cent. of the vaccinated are not immunized.

A striking finding was that among 19 vaccinated patients aged 41 years and upwards there was no death, whereas among 94 non-vaccinated patients belonging to the same age group there were 40 deaths.

John W. D. Megaw.

LEVKOVICH, E. N. [**Active Immunization against European Spotted Fever. Communication I. Adaptation of the Virus of the European Spotted Typhus to the Organism of White Mice.**] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii.* Moscow. 1943, No. 1–2, 33–6. [In Russian.]

—— & PETRISHCHEVA, P. A. [**Communication II. Comparative Valuation of the Effectiveness of Spotted-Typhus Vaccines in Experiments on Animals and in Epidemiological Tests on Man.**] *Ibid.* 36–43. [In Russian.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 218–19.]

DURAND & SPARROW found that prolific multiplication of the rickettsiae of Marseilles fever or murine or epidemic typhus took place in the lungs of white mice that had been infected intranasally and DURAND & GIROUD successfully used such infected lungs for the preparation of typhus vaccine. These results were confirmed by the experiments described in the first paper in which characteristic pneumonia infection, with a large accumulation of *Rickettsia prowazeki*, was produced in white mice by intranasal injection of a centrifuged emulsion of the intestines of lice [*Pediculus humanus*, L.] that had fed on typhus patients, and was subsequently maintained in further mice by similar injection of lung-tissue emulsion. The virulence of the infection was increased by serial passage.

In the second paper the results are given of tests on guineapigs and man of the protection against epidemic typhus afforded by Cox's vaccine (prepared from *R. prowazeki* cultivated in the tissue of the yoke sac of a chick embryo), a vaccine made from infected mouse lung and vaccines prepared by two slightly different methods from the intestines or whole bodies of infected lice. All were efficient, and there was no evidence that one was preferable to another, except that the vaccine prepared from the whole bodies of lice was less satisfactory, as it caused an allergic skin reaction in two instances.

Details are given of the method adopted for rearing the lice in large numbers in order to obtain vaccine from them. They were kept at 30–32°C. [86–89·6°F.] and 85–90 per cent. humidity in small wooden boxes ($4 \times 2\frac{1}{2} \times 10$ cm.) with tightly fitting lids and with bottoms of bolting silk. A piece of muslin folded double was placed over the lice in each container, which would hold 100–150 large adults or twice as many larvae. The lice were allowed to feed for an hour twice daily by strapping the boxes round the hips of women who were immune from typhus. Uninfected lice were not fed on the same woman as infected ones, so that they could not become infected by feeding on the excreta of the latter. Feeding once daily instead of twice reduced the numbers of eggs laid per female from 230–300 to 160–200 and resulted in high mortality of the young lice, which became too weak to suck blood if starved for 15–20 hours after hatching.

The lice usually settled and oviposited on the muslin that covered them. The muslin was renewed weekly when the boxes were cleaned and the old pieces with the eggs were put in fresh ones. Under the conditions of rearing, the rate of mortality was only 2–10 per cent. in the egg stage and 25–35 per cent. during subsequent development, and the life-cycle averaged 19 days. The eggs hatched in 6–7 days. The extremes of temperature at which hatching occurred were 22–23 and 38°C. [71·6–73·4 and 100·4°F.]; practically all newly laid eggs lost their viability in 3–5 days at temperatures below 23°C.

The lice were infected by Weigl's method of rectal injection or by feeding them on typhus patients during the first 4–6 days of illness, the latter method resulting in the infection of about 50 per cent. They were given three or four feeds of an hour's duration on the typhus patients in the course of two or three days, and were then fed on healthy women as before, since, if they were fed on a patient after the sixth day of illness the rickettsiae did not accumulate in them and frequently did not develop at all, being apparently neutralised by the substances that appeared in the patient's blood. A third method of infecting lice, developed by Pshenichnov but not used by the authors, consists in allowing them to feed on the skin of an immune person after it has been smeared with an emulsion of infective material. The temperature and humidity at which the lice were normally reared proved most favourable for the development of rickettsiae in them. The rickettsiae appeared and attained their maximum numbers 5–7 and 14–16 days, respectively, after the lice were fed on the patients.

Pshenichnov, A. V. [**A Universal Method for studying Infections transmitted to Man by Blood-sucking Insects and a New Vaccine against Spotted Typhus.**] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii.* Moscow. 1943, No. 1–2, 43–8. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 219–20.]

The author and his collaborators have devised a method of infecting lice [*Pediculus humanus*, L.] with typhus in large numbers by allowing them to feed through a piece of animal membrane on defibrinated human blood to which has been added an emulsion of infected louse intestine or guineapig brain. The appearance of *Rickettsia prowazeki* in the lice usually occurred after 7–9

days. The blood is warmed to about the temperature of the human body and is kept at slight pressure under the membrane. This method of feeding has also been successfully used by Mitrofanova to infect lice with bacteria, and preliminary work has shown that other blood-sucking insects, and even ticks, will take blood through membranes.

The advantages of infecting the lice in this way over Weigl's method of rectal injection include the avoidance of injury to the lice, the ease with which large numbers can be infected and the fact that immature lice, as well as adults, can be used. A typhus vaccine as effective as that of Weigl was prepared from third-instar lice that had received their infecting feed when they were newly hatched and were then fed once a day on man for 9–10 days. Weigl's vaccine can only be obtained by feeding lice on man twice a day for about a month.

In preliminary experiments, lice were reared from egg to adult when fed exclusively through membranes. In this case, citrated blood proved better than defibrinated blood. In comparison with lice fed on man, however, the duration of development was rather longer, the rate of mortality during moulting was higher, and the surviving females laid fewer viable eggs.

RAÏKHER, B. I. [**Fundamental Principles of the Technique of preparing Vaccine against Spotted Typhus from Intestines of Lice by Pshenichnov-Raïkher's Method.**] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii.* Moscow. 1943, No. 1–2, 48–51. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 220.]

Details are given of the technique used to prepare a typhus vaccine from the third-instar lice [*Pediculus humanus*, L.] infected in the first instar by feeding through a membrane [see preceding paper], with notes on the method of feeding the lice and of obtaining a constant daily supply of them. For the latter purpose, adults were kept at 30°C. [86°F.] and a relative humidity of 70–80 per cent. in glass jars containing chopped human hair, and were allowed to feed on man for 30 minutes twice a day. A ratio of one male to four females secured maximum oviposition and hatching of 96·4 per cent. of the eggs. The hairs with the eggs on them were daily transferred to other jars and hatched in about five days. The newly hatched lice were collected by allowing them to crawl on to small pieces of fabric that had been rubbed against human skin, to which they were attracted by the odour of perspiration.

The infective blood on which the lice were fed was in a small metal box over which a membrane was stretched and held in position by means of a ring. They attached themselves quickly when scattered over the membrane and completed their feed in 15–120 minutes, the time varying with the quality of the membrane employed. Up to 1,500 could be infected simultaneously on each feeding box, and the blood in a box remained infective for at least 24 hours. After infection, they were fed on man once a day. More frequent feeding did not affect the time of appearance or the intensity of the development of the rickettsiae, though it somewhat reduced the rate of mortality among the lice. With one daily feed, however, the rate of mortality did not exceed 30 per cent. during the 10–14 days required for the appearance of the rickettsiae.

SERGENT, Edm. & BÈGUET, M. Conclusions pratiques à tirer d'une expérience d'épouillage par poudrage insecticide faite à Maison-Carrée et l'Arba (Algérie). [**Practical Conclusions drawn from an Experiment in Delousing by Insecticidal Dust.**] *Arch. Inst. Pasteur d'Algérie.* 1944, June, v. 22, No. 2, 109–112.

This is a preliminary account of practical trials of dust insecticides for delousing, carried out in collaboration by Dr. G. K. STRODE and other doctors

of the Rockefeller Foundation, and workers of the Pasteur Institute of Algiers. Two dusts were used ; MYL [pyrethrins, iso-butyl undecyleneamide and dinitro anisole] and DDT [probably at 10 per cent.]. The trials were made (1) on the prisoners at the Maison-Carrée penitentiary, (2) on the villagers at Arba, 30 km. from Algiers.

It was found that one dusting with the DDT dust or two treatments with MYL formula effectively rid a person of lice. It was possible to do the dusting, without undressing the people, by using dust guns to blow the powder under the clothes. For this reason and the innocuous and effective characters of the dusts, these treatments were quite popular among the people treated.

Reinfestation eventually occurred because it is impossible completely to segregate any community, even of prisoners. It is considered to be impossible to rid a district of lice, even by treating hundreds of thousands of people because the lice would finally spread again. The great value of these dusts would be best employed by a mobile disinfesting unit to check typhus outbreaks.

J. R. Busvine.

HARINGTON, C. & YOUNG, E. A. E. **Murine Typhus in the District of Port Elizabeth.** *South African Med. J.* 1944, Nov. 11, v. 18, No. 21, 368–9.

Murine typhus infection has already been detected among rats in many parts of South Africa.

The authors have now isolated murine rickettsiae from rats in the Cape Eastern Province, at a place about 25 miles from Port Elizabeth, and also from a patient on whose farm the rats were caught. It is mentioned that one of the 10 cases of typhus-like fever described by SCROGGIE and GRAY in 1931 occurred in the same locality ; in these ten cases louse transmission was regarded as being excluded but rats and their fleas could not be incriminated.

The present patient had an attack of typhus fever lasting 20 days, the agglutination titre with *Proteus OX19* was 1–800 on the 9th day and 1–6,400 on the 12th day. The reactions with *OX2* and *OXK* were negative. Two similar, and cross-immunizing, strains of orchitic rickettsiae were isolated and passaged at least 20 times through guineapigs ; one strain was obtained from the patient's blood, taken on the 9th day, the other from a pooled suspension of the brains of five rats (*Rattus rattus*) caught on the premises.

Both strains showed cross protection when tested on guineapigs against a murine strain isolated from rats at Paarl in the Cape Western Province by RHODES in 1934 and also against the " Ettie " epidemic strain isolated by GEAR from a patient during an epidemic of louse typhus in the Eastern Transvaal in 1939.

The responses of guineapigs and Cape gerbils to the two strains corresponded closely in those described by GEAR and DAVIS for South-African murine strains.

John W. D. Megaw.

ALICATA, J. E. & BREAKS, Virginia. **Typhus Fever in Honolulu. Certain Epidemiological Aspects.** *Hawaii Med. J.* 1942, Nov.–Dec., v. 2, No. 2, 59–62, 3 figs.

An account is given of a careful survey of the incidence of murine rickettsial infection among the rats of Honolulu, where 202 human cases of murine typhus have been notified during the five-year period 1937–1941.

In May 1941 a strain of rickettsia, immunologically identical with the Wilmington murine strain, was isolated from a patient. Rats were trapped in seven districts of Honolulu—100 in each of five districts and 50 in each of the other two. Brain suspensions from these were injected intraperitoneally

into 249 guineapigs, each animal receiving a pooled suspension from the brains of two or three rats. From 73 of the guineapigs strains of rickettsiae identical with the above were isolated, so that at least as many of the 600 rats must have been infected, a rate of 12·1 per cent.

Among 17 rats from premises in which typhus patients lived, infection was found in eight (47 per cent.).

Human infection must have been acquired chiefly in the homes of the patients rather than in their places of work, because among the 43 patients who had seen rats at their homes or places of work only four had seen the rats at their places of work and not at their homes. Seven other patients had not seen rats at either place.

The brains of 109 cats and 26 dogs from the area were examined with negative results. Fleas collected from six cats and one dog, in houses where human infection had occurred recently, were also negative.

The percentage incidence of rat infection in the seven districts was as follows (the figures in parentheses show the percentage of the 200 human cases that occurred in each of the corresponding districts) :—19 (16·7) ; 8 (2·9) ; 21 (12·8) ; 9 (4·9) ; 3 (3·4) ; 14 (26·7) ; 6 (2·9). *John W. D. Megaw.*

RUIZ SÁNCHEZ, F. Estudios sobre el tifo de Guadalajara. Aislamiento de un virus del tipo murino. [**Studies in Typhus Fever in Guadalajara (Mexico) ; Isolation of a Murine Strain.**] *Medicina.* Mexico. 1944, Sept. 25, v. 24, No. 468, 363–70, 3 figs.

During the 12 years since 1932, when typhus fever was first recognized in Guadalajara, 162 cases have been notified. The seasonal distribution of the disease is remarkably uniform, the cases occur sporadically, all social grades of the community are equally affected, lice are rarely detected on the patients, rats and their fleas are abundant on the affected premises, and the disease is rarely fatal.

The author has now isolated an orchitic strain of rickettsia from a patient, also from the brains of rats caught in the same locality and from fleas collected from the rats.

He concludes that the typhus fever which is endemic in Guadalajara is of the murine, flea-borne, type. *John W. D. Megaw.*

FARNER, D. S. & KATSAMPES, C. P. **Tsutsugamushi Disease.** *U.S. Nav. Med. Bull.* 1944, Oct., v. 43, No. 4, 800–836, 1 fig. [201 refs.]

[An adequate summary cannot be made of this paper which in itself is an admirable summary of what is known, and believed, with regard to the mite-borne tsutsugamushi disease, now often called scrub typhus.]

The authors define the disease as "one of the typhus group of diseases caused by *Rickettsia tsutsugamushi*, transmitted by the bite of a larval trombiculid mite." They provisionally assume that the fever is primarily a widespread disease of several (or many) species of vertebrates in Asia and Australasia. The vector mite never feeds more than once on an animal host and, therefore, cannot transmit infection by its own bite, but the offspring of the infected mite may acquire infection through the ovum and so be able to transmit the disease on the one occasion on which they bite.

The paper contains a fully documented account of the long and confused history of the disease, which was first described by a Chinese writer in the 3rd century, A.D., and was attributed by him to the bite of a minute red insect,

presumably a mite. For many years the people of certain riverine areas in Japan have known the existence of the disease and have regarded it as being caused by the bite of a mite which they call *akamushi*.

In the section on the reservoir hosts it is stated that final proof of the transmission cycle has been established on only one occasion, when the rickettsia was isolated from a field vole, *Microtus montebelloi*, and also from the mite, *Trombicula akamushi*, which was found capable of transmitting infection from the vole to man.

The bibliography contains references to 201 articles consulted in the preparation of the paper; these articles have been selected from a list several times longer. Although the paper is not lengthy, it is so closely packed with information that it really constitutes a monograph on the basic aspects of the disease. Room has been found for many explanatory and critical comments which add greatly to the value of the paper. A useful feature is a glossary with explanations of more than 50 of the names that have been applied to the disease; and this lengthy list is said to be by no means complete. The existence of so many names is an index of the confusion that has surrounded the disease up to recent times. This confusion is at first sight surprising because the disease appears to be strictly unitary, being caused by one species of rickettsia and transmitted by closely related species of mites. The chief misunderstanding has been due to the fact that the occurrence of a local sore and associated adenopathy was long regarded as an essential feature of the classical tsutsugamushi disease so that the absence of local lesions was considered to rule out the diagnosis of this fever.

[It is interesting to find that 24 of the synonyms of the disease include a reference to the arthropod vector, and 16 contain the word typhus, so it seems fair to suggest that the name mite typhus which combines a reference to the vector and the clinical type of the disease has decided advantages.]

The authors point out that the disease described by SCHÜFFNER in 1910 as "pseudotyphus" ought to be called pseudotyphoid in English, as was done by Schüffner himself in his papers in English on the disease. Many authors fail to realize that what the Germans call [abdominal] typhus is called typhoid by writers in English.

Only one trifling error has been noticed in the paper; the authors state that the name mite typhus was proposed as being "parallel to flea typhus (endemic typhus), louse typhus and tick typhus," but the existence of flea typhus was not known till several years after 1921 when the reviewer suggested the names mite typhus, louse typhus and tick typhus; he later suggested the name flea typhus as being more suitable than murine or endemic typhus.

The description of the geographical distribution of the disease is admittedly based on the assumption that an *OXK* type of agglutination response is reliable evidence that a case of fever is tsutsugamushi disease. The authors appear to accept this assumption though they point out that the agglutination of *OXK* by the serum of animals is not sufficient evidence that these animals are infected by *R. tsutsugamushi*; they also quote an example of the isolation of *Proteus OXK* from an animal in which this type of response occurred. The *OXK* reaction is invaluable as an aid to diagnosis but the question still remains whether it can be relied on for the identification of mite-borne typhus in circumstances in which there is no other evidence of the existence of this disease.

[Research workers on the typhus fevers will be specially grateful to the authors, who, at the cost of great labour, have provided an admirable work of reference on the basic problems connected with mite-borne typhus. But the paper ought also to be read by every medical man working in the East, and particularly by medical officers serving in areas in which the disease is of major military importance.] *John W. D. Megaw.*

LOGUE, J. B. **Scrub Typhus. Report of Epidemic in the Southwest Pacific.** *U.S. Nav. Med. Bull.* 1944, Oct., v. 43, No. 4, 645–9, 1 chart.

This is a brief account of an outbreak of mite-borne typhus in an island in the South-West Pacific area. Among an unstated number of U.S.A. troops there were 230 cases and 22 deaths within a period of less than four months. The troops landed on December 26th, 1943, and the first case occurred four days later. Within a month the peak period of incidence was reached; 38 cases occurred during the week ending February 5th. Then a steady decline set in, and there were only three cases during the first week of April. The troops departed from the island on April 30th, having had no fresh cases during the previous 17 days.

The troops were working and bivouacking on wet ground covered with *kunal* grass growing to a height of 10–20 feet. The preventive measures, which proved effective, were :—(1) Selection of well drained camps whose sites had been burned down beforehand when this was possible. (2) Sometimes the only practicable preparation of the site consisted in the removal of grass, shrubs, leaves, and rubbish, from the sites and paths. (3) Tent sites and paths were sprayed with thin oil, and orders were given to the men to keep to the prepared paths, and to avoid sitting down on the ground. (4) Rat control was on the same lines as in plague prevention. (5) Dimethylphthalate repellent was applied to the legs and worked well into the clothing from the waist to the feet. Insecticide powder was applied round the waist and ankles, also inside the boots and leggings. After excursions into infested areas, the clothing was removed, and the whole body, except the genitalia, was lightly rubbed with a cloth moistened with kerosene; then clean clothing was put on.

The incubation period was 4–18 days. The typical eschar and regional adenopathy were usually present. Apart from the occurrence of these and of "relative leucopenia" the clinical features of the disease do not seem to have differed in any essential respect from those of louse-borne typhus. The treatment was "supportive," by intravenous fluids, plasma, and small transfusions of blood. Oxygen was useful in serious cases; penicillin was not found effective. Convalescence was very prolonged; weakness and palpitation persisted after several months of rest, and it was suspected that permanent myocardial damage might result from the disease.

The mortality rate is said to have been higher among Japanese troops exposed to similar conditions.

Certain damp coastal areas were found to be specially dangerous; high-lying and well-drained ground was relatively safe even when covered with the same kind of grass. *John W. D. Megaw.*

KORSHUNOVA, O. S. [**Etiology of Tick Spotted Typhus in Krasnoyarsk Province.**] *Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii.* Moscow. 1943, No. 1–2, 59–64, 7 graphs. [In Russian.]

KRONTOVSKAYA, M. K. & SHMATIKOV, M. D. [**On the Epidemiology of the Tick Spotted Typhus of Central Siberia.**] *Ibid.* 65–8. [In Russian.]

BOCHAROVA, T. V. [**On the Epidemiology of the Tick Spotted Typhus.**] *Ibid.* 68–72, 1 graph. [In Russian.]

[Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 220–21.]

In the first paper an account is given of investigations on the causal agent of a disease transmitted by *Dermacentor nuttalli*, Olen., epidemics of which occurred in spring and summer in the Province of Krasnoyarsk (central Siberia). It is called tick-typhus, since its symptoms were similar to those of epidemic typhus. It proved to be pathogenic to guineapigs, rabbits and monkeys, but not to

white rats. Rickettsiae were observed in the tunica exudate of the guineapigs, and the rabbits and monkeys gave a positive Weil-Felix reaction, which was most marked with Proteus OX19. Cross-immunity tests demonstrated the identity of the strains of the causal agent isolated from different patients, from examples of *D. nuttalli* collected in a focus of the disease, and from ground-squirrels [*Citellus*]. A strain from man immunised guineapigs against Marseilles fever, but not against a guineapig strain of epidemic typhus. On the other hand, the last strain conferred almost complete immunity from the tick-typhus strain, while Marseilles fever conferred none.

Much of the information in the second paper is similar to that already noticed. Investigations in central Siberia revealed a focus of tick typhus of three years' standing in a steppe district where *D. nuttalli* was practically the only tick found. It occurred in areas overgrown with grasses, the adults were abundant on cattle, and numerous larvae were taken early in July on *Citellus eversmani* and *Stenocranius* (*Microtus*) *gregalis*. The other ticks found were *D. silvarum*, Olen., and *Ixodes persulcatus*, Schulze, but they occurred in negligible numbers, and *I. persulcatus* was confined to places covered with woody vegetation, where the adults were taken on cattle, horses, dogs and cats. Natural infection was found to be prevalent in *D. nuttalli*, and guineapigs contracted the disease when the ticks were fed on them. Possible measures for the control of ticks are discussed. They include the burning or mowing of grass, the application of sprays, the dipping of cattle and measures directed against the rodent hosts.

In the third paper is recorded the finding of several foci of tick-typhus in eastern Siberia where areas overgrown with low woody vegetation or tall and dense grass provided favourable conditions for ticks and rodents. All the infected persons had been bitten by ticks, and the numbers of cases were greatest in localities in which ticks were most abundant. Natural infection was demonstrated in *Eutamias asiaticus*, *Cricetulus furunculus*, *Microtus michnoi*, *Apodemus agrarius* and the house rat, *Mus* (*Rattus*) *norvegicus*, and also in a large proportion of larvae of ticks on rodents and of adults on cows and dogs. The infection in larvae suggests that the causal agent persists in ticks from one generation to the next, and this view is supported by experiments by workers in central Siberia in which guineapigs were infected by inoculation of eggs laid by ticks taken in the field, and also by the bites of the larvae and nymphs of ticks, including *D. nuttalli*, *D. silvarum* and *Haemaphysalis concinna*, Koch. Suggestions similar to those in the second paper are made for tick control.

YELLOW FEVER.

AFRIQUE OCCIDENTALE FRANÇAISE: RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1942 [DURIEUX, C.]. pp. 53–69. Service de la fièvre jaune. [**Yellow Fever Service.**]

The preparation of yellow fever vaccine follows the methods previously described [see this *Bulletin*, 1940, v. 37, 92, and 1942, v. 39, 761]. The virus employed had undergone 255 to 257 passages in mouse brain and its characters had not varied during the period under consideration. During 1942, a total of 3,238,500 doses of yellow fever vaccine had been prepared and in addition 33,680 ampoules of 2 per cent. gum arabic for use in making suspensions of the dried vaccine. It is recommended that any vaccine not used within half an

hour of preparing the suspension should be rejected. Nevertheless, the vaccine is evidently able to withstand considerable vicissitudes, for a consignment that had been broken en route, was examined for virulence after being at temperatures of 30°C. and over for at least six weeks under unfavourable conditions, and the virus killed two out of three mice in dilutions of 1 : 1,000,000.

A total of 2,913,114 persons were inoculated either subcutaneously or by scarification during the year, and it is estimated that by the end of 1942 a third of the total population of French West Africa had been vaccinated against yellow fever. The results of protection tests with the sera of vaccinated persons showed that after less than one year 2,207 out of 2,305 were positive ; after one year, 49 positive out of 49 ; and after two years 10 positive out of 10 examined.

The pathological anatomy department examined the livers of 34 persons suspected of dying of yellow fever ; of these nine were positive. The following rapid method of preparing tissues described by POURSINES and DEZEST (*Médecine Tropicale*, 1942, No. 2, p. 120) has been adopted, as sections can be prepared within 150 minutes.

Tissues from cadavers are sent to the laboratory in 5 per cent. formalin. They are then cut into pieces 1 mm. thick and fixed in Dubosq-Brazil, alcoholic picro-formol [picric acid 1 gm. ; formol 60 cc. ; glacial acetic acid 15 cc. ; 80 per cent. alcohol 150 cc.] at 56°C. for 15 minutes ; passed through seven changes of alcohol, each of 5 minutes at 37°C. ; passed through seven similar changes of xylol at 37°C. ; finally passed through three baths of paraffin wax each of 10 minutes. The blocks are then cut and the sections fastened on to the slides by means of gelatin (16 minutes) and then stained with haematein-eosin-safranin.

During the year 10 cases of yellow fever, nine fatal, were diagnosed, including seven Europeans and three Africans. Details are given of eight of these cases. The patients all lived in sparsely populated areas and, with one exception, there was no relation between the various cases either in time or locality. The epidemiological evidence supports the view that at least 8 of these cases were probably examples of jungle yellow fever. Six of the ten had not been vaccinated against yellow fever ; two had been vaccinated some time previously ; in the remaining two, both Africans, it was uncertain whether they had been vaccinated or not.

The cause of these occasional failures to develop immunity after vaccination is discussed and it is considered that they may be due to the vaccine being rubbed off before the virus has had time to pass through the cutaneous scarifications. In order to avoid this possibility the vaccine, after being deposited on the skin, is kept under observation until it dries, when the contained gum arabic forms a protective covering. *E. Hindle.*

ELLIOTT, M. **Yellow Fever in the recently Inoculated.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Dec., v. 38, No. 3, 231–4, 1 chart.

The author gives details of three cases of yellow fever which came under his care, and are of interest since at that time (June 1942) they were the only cases that had occurred among British and Allied troops since the beginning of the war.

All three men had received preventive inoculation at least two years earlier. In two cases there was a severe clinical course and rapid onset of death, suggesting that the initial immunity against yellow fever was slight. All three developed the disease in West Africa.

It is noted that at least 135,000 people received preventive inoculation between January 1941 and June 1942, therefore the prophylactic value of the

anti-yellow-fever inoculations has been proved beyond question, and the catastrophic annihilation of large numbers of white troops may have been prevented. *E. Hindle.*

De Assumpção, L. Relações imunitárias entre febre amarela e outras infecções clìnicamente parecidas que se observam nos climas tropicais e subtropicais. [**Immunity Relations between Yellow Fever and Diseases resembling it Clinically in the Tropics and Subtropics.**] *Arquivos de Hig. e Saúde Pública.* São Paulo. 1944, Sept., v. 9, No. 22, 19–32. [22 refs.]

The author first gathers together the evidence which shows that the viruses of urban, rural and jungle yellow fever are identical, and that laboratory animals immunized against one are immune to the others. He then takes up the question of dengue, Rift Valley and sandfly fevers as a group of diseases which may be confused with yellow fever. As regards *dengue* he quotes Jorge as saying that " the similarities are more apparent than real " [whatever that may mean]. It seems strange that anyone acquainted with both dengue and yellow fever would ever confuse them ; anyway the protective test and absence of cross-immunity would soon set the matter at rest. Next, *Rift Valley fever* ; animals such as cattle, sheep, goats, susceptible to Rift Valley fever are not susceptible to yellow fever and there is no cross-immunity between the two diseases. The author quotes the case, reported by Findlay and MacCallum, of a laboratory assistant who had an attack of yellow fever in 1931 and of Rift Valley fever in 1934, both viruses being isolated from his blood. The similarities between the two diseases are certainly striking in man : clinically, the symptoms of the former are like those of yellow fever, both produce liver necrosis with intranuclear inclusions and Councilman lesions, both give rise to lasting immunity and both are transmitted by *Aëdes*. But there is no true cross-immunity between them, though the *interference phenomenon* may be seen, as Findlay and MacCallum [this *Bulletin*, 1937, v. 34, 689] have demonstrated. Of 10 *Macacus rhesus* inoculated with the two pantropic viruses, intraperitoneally or subcutaneously, seven were protected ; camondongos inoculated with neurotropic yellow fever virus and with pantropic Rift Valley virus lived longer than after inoculation with either singly, and some might survive ; but no protection is afforded if the Rift Valley fever virus is inoculated 24 hours before the yellow fever virus.

Though an attack of *sandfly fever* imparts a certain degree of immunity against a second attack in the succeeding season, this immunity is not lasting and there is no cross-immunity between it and yellow fever.

Lastly, *spirochaetal jaundice* may be confused clinically with yellow fever [as the classical studies of Noguchi proved], but laboratory tests—finding of the *Leptospira* in the blood or the urine, agglutination results and animal inoculation—will suffice to differentiate and there is no cross-immunization with yellow fever virus. *H. Harold Scott.*

Linhares, H. Inoculação de virus amarílico em gatos jovens. [**Inoculation of Yellow Fever Virus in Kittens.**] *Mem. Inst. Oswaldo Cruz.* 1943, Apr., v. 38, No. 2, 201–7. English summary.

" 1. Young cats inoculated intracerebrally with relatively large doses of neurotropic or viscerotropic virus, and intraperitoneally with viscerotropic virus, fail to show circulating virus up to 12 days post inoculation.

" 2. Such cats also fail to show symptoms referable to the virus.

" 3. It was impossible to isolate virus from the brains of inoculated cats dying in the course of the experiments, and histological examinations of the brains failed to show encephalitis (only one case with toxic encephalitis).

"4. The development of serological immunity after 30 days was observed in all but two of the cats inoculated intracerebrally or intraperitoneally with neurotropic virus; with Asibi strain, only two positive results were obtained by the intracerebral route.

"5. Young cats are relatively insusceptible to yellow fever virus, only giving the reaction of immunity."

LINHARES, H. Suscetibilidade de camondongos ao virus amarílico administrado por vias extraneurais. [**Susceptibility of Mice to Yellow Fever Virus administered Extraneurally.**] *Mem. Inst. Oswaldo Cruz.* 1943, Apr., v. 38, No. 2, 209–24. [10 refs.] English summary.

"1. French neurotropic, Asibi and vaccine (17D) virus, infect young mice (21 days) when instilled in the nostrils, killing them with symptoms of encephalitis, or developing immunity.

"2. French neurotropic virus and Asibi (and perhaps vaccine virus), when instilled in the ear of young mice, may infect them, producing development of immunity.

"3. After instillation in the scarified cornea of young mice, French neurotropic virus, Asibi and perhaps vaccine virus, may produce infection. If the cornea, however, is undamaged, it has not been found possible to infect mice in this way.

"4. French neurotropic virus, Asibi, vaccine, Asibi Egg I and Egg III introduced into the stomach, may infect young mice, causing a fatal encephalitis or rendering them immune.

"5. It is possible to infect mice 0–6 days old by simple deposition of virus or rubbing the suspension on the whole or scarified skin."

LINHARES, H. Suscetibilidade de pintos ao virus amarílico neurotrópico. [**Susceptibility of Chicks to Neurotropic Yellow Fever Virus.**] *Mem. Inst. Oswaldo Cruz.* 1943, Apr., v. 38, No. 2, 225–51. English summary.

"1. After 80 serial passages from brain to brain of chicks, neurotropic virus fails to show essential modifications in the behaviour of the virus in mice or chicks.

"2. Chicks are susceptible by intracerebral, intraperitoneal and intradermal route, showing high levels of circulating virus and become immune when inoculated during the first days after birth. But circulating virus varies, however, in inverse ratio to age. It does not seem possible to infect chicks by the gastric route.

"3. During the first days virus may be found occasionally in the lungs, liver, spleen and kidneys; some days afterwards, no chicks showed virus in other organs than brains, in which virus persists up to 10th day post-intraperitoneal inoculation and up to 15th day after the intracerebral inoculation, and perhaps till later. We have, however, not been able to isolate the virus from excretions.

"4. There does not seem to be any difference in susceptibility to the yellow fever virus in chicks with B avitaminosis.

"5. Detectable immune bodies appear 10–11 days after intraperitoneal and intracerebral inoculation, at a time when many of the chicks still have virus in the brain.

"6. Age has a marked influence on the development of immunity, in chicks inoculated by intraperitoneal route.

"7. The multiplication and circulation of virus after intradermal inoculation of 50 to 160 M.L.D. renders possible the suggestion that infected mosquitoes can diffuse the virus among chicks and, perhaps, other birds, a few days old."

LINHARES, H. Transmissão de imunidade antiamarílica da mãe aos filhos, em camondongos. [**Transmission of Yellow Fever Immunity from Mother to Offspring in Camondongos.**] *Mem. Inst. Oswaldo Cruz.* 1943, Apr., v. 38, No. 2, 187–200, 2 charts. English summary.

An interesting and important article, recalling, confirming and amplifying work of ten years ago which, if not forgotten, has at least tended to recede into the background. In 1934, HOSKINS [this *Bulletin*, 1934, v. 31, 840] showed that yellow fever antibodies were transmissible in *Macacus* across the placenta, and probably also *via* the milk, and in the same year STEFANOPOULO [*ibid.*, 842] showed the same to hold good for camondongos, and two years later STEFANOPOULO, LAURENT and WASSERMANN proved that blood from the umbilical cord and also the milk of immune mothers contained protective antibodies [this *Bulletin*, 1937, v. 34, 346].

In the present paper the author has, by series of carefully planned experiments, verified these results and demonstrated how early immunity is transmitted and for how long it persists. The camondongo is a good animal for experiment because it is easily reared in the laboratory, it has fairly numerous progeny, the gestation period is short, growth of the young is rapid and they are easily handled.

Active immunization was performed by subcutaneous inoculation of the mother with 0·12 cc. of 15 per cent. suspension of neurotropic virus of camondongos moribund from yellow fever encephalitis; passive immunization by injection of hyperimmune Rhesus serum. Immunity in the mother was verified by intracerebral inoculation of 0·03 cc. of 2 per cent. starch emulsion with 0·2 cc. intraperitoneal injection of 15 per cent. suspension of neurotropic virus. In the offspring, up to 17 days 0·01–0·32 cc. of the same virus subcutaneously was used; those 21 days old received 0·03 cc. intraperitoneally; those over 21 days old were inoculated in the same way as the mother. Abundant controls were used throughout the experiments.

The following sets of experiments were carried out: First, the offspring of immune mothers were shown to be immune, but no evidence was found to indicate that the *virus* passed either *via* the placenta or the milk; consequently it follows that the immunity conferred is passive. Second, by another series of experiments it was shown that antibodies traverse the placenta. Four females gave birth to young about 20 days after being inoculated with the virus and the young were taken away and suckled by non-inoculated mothers who had just had young. Twenty-one out of 23 inoculated with virus survived, whereas all but two of 22 normal young died. Thirdly, females were inoculated with the virus on the day of parturition and suckled their offspring for 21 days; at the end of that time the latter were found to be immune, showing that antibodies had passed in the milk of the mothers and had been absorbed in the intestine of the young.

Next, the author took two lots of females and to one lot virus was administered. Both lots parturated about 25 days later and the offspring of the immunized mothers were suckled by the non-immunized and *vice versa*. Twenty-one days later 96·4 per cent. (108 out of 112) of the normal offspring suckled by the immunized mothers were immune, but only 10 per cent. (11 out of 109) of the offspring of the immunized mothers suckled by the unimmunized.

Further experiments showed that transplacental immunity was of brief duration, diminishing rapidly after birth and disappearing altogether by the

eleventh day. Also that immunity acquired through the milk is slight at first and increases up to the tenth day, and animals so fed remain immune for another eleven days, or, if suckling is continued, as long as lactation lasts. Finally, camondongos passively immunized by injection of serum of hyper-immunized Rhesus monkeys transmit a temporary immunity to their offspring by way both of the placenta and of the milk. *H. Harold Scott.*

PLAGUE.

LE GALL, R. La peste à Madagascar. [**Plague in Madagascar.**] *Bull. Office Internat. d'Hyg. Publique.* 1943, July–Aug., v. 35, Nos. 7–8, 318–48, 2 charts & 1 map.

A detailed account, with abundant figure data, is here given of 20 years of plague in Madagascar between 1921 and 1941. Plague appeared on the coast at various points as early as 1899, but always disappeared spontaneously until the disease obtained a footing on the central uplands at Tananarivo, when it became endemic. A record of the "index of contamination," or number of cases per 10,000 inhabitants, shows 14·2 for 1921 and even higher figures year by year to 1932 with 30·4 and 1936 with 14·4, after which a marked decline took place, exemplified in annual figures from 6·6 to 1·8. This diminution is directly claimed as due to the introduction of large scale vaccination with living E.V. plague bacilli. Plague appears in three forms, pneumonic, septicaemic and bubonic. The septicaemic form, a bacteraemia, is in general terms only a terminal feature of either pneumonic or bubonic plague. Pneumonic plague is rather common in the high plateau region and is explainable as a respiratory disease of direct infection and due primarily to climatic conditions, in other words to the lowering of the temperature at least to below 15°C. [59°F.], which is winter in the island. Plague, as judged by mortality returns, has a high mortality of about 91·2 per cent., which, however, is a doubtful figure owing to the likelihood of concealment of cases by the natives, as far as possible. This is borne out by the statement that some 95 per cent. of cases of plague are only diagnosed by organ smear *post mortem.*

The author has little doubt that the main vector of plague is the rat flea *Xenopsylla cheopis*, and also stresses the fact that this flea can live in burrows, in dark corners, in rice débris, and in dust, altogether away from its host, the domestic rat. The rôle of man in the dissemination of plague appears to be secondary. A rat flea index too, with the knowledge of possible existence of the flea apart from its host, has become of much less interest to the epidemiologist. Continued examination of captured rats for plague infection seems to be superfluous and has been given up as a laboratory procedure. Out of 87,105 rodents examined between 1931 and 1935 only 0·12 per cent. were found to be carriers of plague bacilli.

It is natural that great emphasis should be placed in a review of plague in Madagascar on the prophylactic value of the E.V. vaccine of GIRARD and ROBIC [see this *Bulletin*, 1943, v. 40, 777; 1939, v. 36, 314]. Some striking figures are given of the reduction of incidence of plague after its introduction. Take the five years before it came into use, 1930 to 1934, with incidence per 10,000 population respectively of 13·1, 28·9, 30·4, 28·4 and 25·8, and compare them with those of five years when it was in use, 1937 to 1941, with the figures 6·6, 4·5, 4·7, 5·2 and 1·8. In fact the author roundly declares that the killed vaccine of the Pasteur Institute of Paris (previously used) was inefficacious. Treatment of plague has been on the lines of use of E.V. anti-plague serum or

serum and sulphonamide, especially sulphapyridine, with excellent results in bubonic plague and no value in pneumonic plague. In conclusion the hope is expressed that plague, like smallpox, will soon have disappeared from the Great Island. *W. F. Harvey.*

WOODWARD, Gladys E. **The Ribonuclease Activity of** *Pasteurella pestis* **(Plague Bacillus).** *J. Biol. Chem.* 1944, Nov., v. 156, No. 1, 143–9. [13 refs.]

What is shown by the data of this report is that living *Pasteurella pestis*, cells killed by phenylmercuric nitrate, and a cell-free preparation decompose the ribonucleic acid of yeast and that the predominant action appears to be depolymerization. In the author's summary this is stated as follows:—"Analytical data, obtained from hydrochloric acid precipitation and uranium fractionation, show that yeast nucleic acid is enzymatically decomposed by living cells of *Pasteurella pestis*, cells killed by phenylmercuric nitrate and by a cell free preparation. Only part of the nucleic acid decomposed is hydrolyzed to mononucleotides, the remainder probably existing in a depolymerized state." *W. F. Harvey.*

HECHT, O. Consideraciones entomológicas a la epidemiologia de la peste bubónica de los roedores en Venezuela. [**Entomological Notes on the Epidemiology of Bubonic Plague in Rodents in Venezuela.**] *Rev. Sanidad Asistencia Social.* Caracas. 1943, v. 8, No. 6, 1159–62. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 231.]

Details are given of the monthly collections of fleas from rodents trapped between March 1942 and June 1943 in the sylvatic zone of Aragua State, Venezuela, referred to in a previous paper. *Rhopalopsyllus* formed 81·9–100 per cent. of the total in each of the 14 months for which records are given except May 1942. It then constituted only 27·5 per cent., *Xenopsylla cheopis*, Roths., and *X. brasiliensis*, Baker, forming 20·3 and 52·2 per cent., respectively. The significance in relation to the transmission of plague of this occasional appearance of species of *Xenopsylla* in considerable numbers is discussed with special reference to the work of Eskey. A small epidemic of plague in man (19 cases) occurred not far away in July and August 1943. The percentage of *X. brasiliensis* had risen in June to 17·3 in the whole area and to 44·9 in the nearest sector, but it was not possible to determine whether the two facts were related.

AUGUSTSON, G. F. **The Flea Genus** *Thrassis* **and Sylvatic Plague, with the Description of** *T. brennani* **n. sp.** *J. Parasitology.* 1944, Aug., v. 30, No. 4, 237–40, 3 figs.

BRAMBELL, F. W. R. & DAVIS, D. H. S. **The Normal Occurrence, Structure and Homology of Prostate Glands in Adult Female** *Mastomys erythroleucus* **Temm.** Reprinted from *J. Anatomy.* 1940, Oct., v. 75, Pt. 1, 64–74, 6 text figs. & 5 figs. on 1 pl. [14 refs.].

—— & ——. **Reproduction of the Multimammate Mouse** (*Mastomys erythroleucus* **Temm., of Sierra Leone.** Reprinted from *Proc. Zool. Soc. of London*, Ser. B. 1941, v. 3, 1–11, 2 text figs. & 7 figs. on 2 pls.

The multimammate mouse of S. Africa (*Mastomys coucha*) is an important link between field and domestic rodents in the transmission of plague. *M. erythroleucus* may in the future be important in this matter, and for those who may be called upon to study this rodent these two papers have their interest. *Charles Wilcocks.*

HUNDLEY, J. M. & NASI, K. W. **Anti-Plague Measures in Tacoma, Washington.** *Pub. Health Rep.* Wash. 1944, Sept. 22, v. 59, No. 38, 1239–55, 4 figs.

Up to 1942 plague had not been declared in Tacoma. Its discovery in this year seems to have been something of an accident and due to the visit of a mobile unit of the United States Public Health Service, " in the course of a routine check for the presence of plague infection." This unit trapped 257 rats " near two large flour mills on the western waterfront of Tacoma harbor " and seven rats were found, by isolation of the plague bacillus, to be infected. The authors admit that " it might be assumed that the plague had been present . . . for many years " and, yet, no human case of plague by the records "has ever occurred in Tacoma." What is most interesting in this record is that active measures were taken immediately, as is obligatory under the Pan-American Sanitary Treaty, " when plague is present in a seaport city." A full description of the measures taken is given : the preliminary survey and the control measures —such as trapping, poisoning, gassing, fumigation, food sanitation, harbourage elimination, rat proofing, quarantine and educational activities. These measures were crowned with success and at the very low cost of 56,742 dollars for the year. Compare this expenditure, in which trappers were paid the high figure of 200 dollars a month, with that of San Francisco for 11 months, 561,143 dollars, Oakland of 65,000 dollars, and Seattle 65,000 dollars. Moreover, about 5,000 dollars of the expenditure remains in capital equipment for a future permanent programme.

" On May 4, 1943, the last positive specimen was found. Since then, more than 8,000 rodents and their ectoparasites have been examined without detecting the presence of plague. It therefore seems reasonable to conclude that the infection has been brought under complete control and that plague has been eradicated in Tacoma." *W. F. Harvey.*

CHOLERA.

ROGERS, L. **Cholera Incidence in India in relation to Rainfall, Absolute Humidity and Pilgrimages ; Inoculation of Pilgrims as a Preventive Measure.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1944, Nov., v. 38, No. 2, 73–89. Discussion 89–94 [GILL, C. A. ; JAMES, S. P. ; COLLINGWOOD, F. C. ; ROGERS, L. (in reply).]

Two distinct parts constitute this paper. It follows the lines already made familiar by the extensive researches of Sir Leonard Rogers which have resulted in the formulation of positive factors in the spread of cholera in India. As the timing of pilgrimages is known and rainfall and absolute humidity are measurable, they have undoubtedly provided a most important method of forecast of the outbreak of cholera on an epidemic scale. All sanitary authorities in India will use this helpful approach to the problem. Rogers brings, with proper emphasis, new and additional data to uphold his contentions, and statistical students of epidemiology, as well as practical sanitarians, will study his tables and explanations very carefully to determine the concordance of calculated and observed figures. The sanitarian in India will take note of the condensed conclusion. " A close watch on the June to October south-west monsoon rains enables high cholera incidence to be foreseen in the autumn months in the endemic areas with absolute humidities always over 0·400 and several months before the spread of epidemics of cholera in the next spring from the endemic to the epidemic areas. The danger of cholera being spread by the return of

pilgrims from any particular Fair can also be foreseen from the climatic data at the time and a knowledge that cholera is present in the areas through which the pilgrims have to travel. . . ."

A somewhat lively and very interesting discussion took place after the reading of the paper, which was concentrated for the most part on the practical expediency and the efficacy of cholera inoculation as a preventive of devastating outbreaks. Colonel GILL touched lightly on the bionomics of the cholera vibrio in his reference to transmission of cholera through the agency of importation by sacred water or sweetmeats. In respect of cholera vaccine, however, he bluntly says of the vaccine of his own time that "cholera inoculation gave no sort of solid immunity." The people of the Punjab do not like compulsion, and the large-scale compulsory plague inoculation in the Punjab of earlier days came to a sudden unfortunate end, with riots and bloodshed. That large-scale trial would have afforded some very useful data, if it had been completed. Colonel JAMES, with his own personal experience of cholera inoculation, which was also that of Colonel Gill, continued the adverse commentary, beginning with the remark that "the material with which Haffkine made the first anti-cholera inoculations in Bengal in 1896" was probably less effective than the vaccine now available. [This is interesting in view of the stress which is now being laid upon the use of living instead of dead vaccines in prophylaxis of other diseases. Some of Haffkine's earliest vaccines were composed of living organisms.] A very important addition to the discussion, contributed by James, is embodied in the remark: "Cholera is the best example of a tropical epidemic disease which is amenable to improvements in environmental, domestic, and personal sanitation. Everyone agrees that India is greatly in need of improvement in those respects as well as in getting more and better food, more and better education and a higher standard of living generally." [It is surprising that the discussion did not elicit any remarks on the possibility of cure being better than prevention, that is to say of the possibility that curative drugs may be discovered which may prove better than a prophylactic inoculation on any compulsory large and expensive scale.] *W. F. Harvey.*

FELSENFELD, O. **The Lecithinase Activity of Vibrio Comma and the El Tor Vibrio.** *J. Bacteriology.* 1944, Aug., v. 48, No. 2, 155–7. [13 refs.]

Sensitive tests are now applied in the examination of lecithinases. Three types, A, B and C have been named. In the present study four *V. cholerae* strains and one *V. El Tor* were available and the lecithinase activity of all these vibrios showed the effects of lecithinase B, choline-phosphatase and glycerophosphatase "resulting in the production of free phosphate choline and fatty acids." The optimal temperature for this activity was 36–38°C. and the optimal *p*H 7·4 to 7·6. Stimulants of the reaction were found in Ca and Mg, but sulphonamides and barbiturates were without effect. Formaldehyde, phenol and fat-soluble narcotics exercised an inhibitory action. "Whether this effect of formaldehyde helps to explain the mechanism of the detoxication of culture filtrates (toxins) through formol, remains to be investigated."

W. F. Harvey.

INDIAN MED. GAZ. 1944, Oct., v. 79, No. 10, 477–9, 5 figs. **Intravenous Transfusions in Cholera and other Conditions. A Note on Technique.**

In cholera cases where collapse and dehydration figure prominently, it may be quite a difficult matter to get the transfusion nozzle into a vein in the usual way. The method here described is one of operation to expose the vein, is very simple and is fully illustrated. It has long been used in the cholera wards of the Campbell Hospital, Calcutta. After exposure of the vein two ligatures are

applied above and below the position of entry. The lower ligature only is tied. The vein is then transfixed from side to side with a surgical needle curved on the flat, so as to pass clean through the lumen. An incision is made through the vein on the needle, also from side to side, and the needle withdrawn. The eye of the needle is used to lever up one lip of the opening to facilitate the insertion of the transfusion nozzle and the upper ligature is tied lightly over the nozzle. It seems probable that this rapid, simple and effective method might be of use in other conditions where entry into a vein is difficult. *W. F. Harvey.*

GRIFFITTS, J. J. **Mouse Protective Antibodies in Human Serums following Injections with Cholera Vaccine.** *Pub. Health Rep.* Wash. 1944, Oct. 20, v. 59, No. 42, 1374–84, 1 fig.

In war time large numbers of men become exposed to the risk of infective diseases who would not ordinarily have to face any such risk throughout life. One of the regular methods employed to counter the risk, both in the last war and in this, has been prophylactic inoculation of vaccines. A quantitative assessment of the value of this vaccination is very desirable and—apart from statistical results—is usually measured in terms of antibody response. Most convenient is the measurement of agglutinin titre, which was done in this case on 34 white male medical student volunteers of 21 to 36 years of age, vaccinated with Inaba and Ogawa strains in equal amounts. One objection to the use of the agglutinin titre is that it may not be a sufficiently true measure of immunity. The author has departed from this stereotyped measure by carrying through, with the human sera, mouse-protection tests, which can be truly said to be a measure of protection. The test consisted in the inoculation of the serum intraperitoneally, and, one hour later, of varying doses of living vibrios in mucin also intraperitoneally, according to the methods of SILER and others of the United States Army Medical School. Results may be summarized as follows :—"Mouse protective substances appeared in the serum of human volunteers 1 week following vaccination. These antibodies were present at least 18 months after vaccination and were more concentrated in serums at 1 week and 1 month than at 3 or 6 months. . . . In this study no definite correlation between height of agglutinin and mouse protective titers could be made." *W. F. Harvey.*

BACILLARY DYSENTERY.

FINERMAN, W. B. & WEISS, J. E. **Control of Bacillary Dysentery in a Tropical Outpost. Report of 1,000 Cases.** *Bull. U.S. Army Med. Dept.* 1944, Oct., No. 81, 71–82.

The point of particular interest in this report on bacillary dysentery concerns the effect of increasing the dosage of sulphaguanidine. The predominant organism, isolated on S.S. or desoxycholate-citrate agar, was *Bact. flexneri*, and cases were classified as mild, moderate or severe "dysentery" or "enteritis" according as a specific dysentery organism was or was not isolated on admission. In the first series of cases, the daily dosage of sulphaguanidine was 6–7 gm., continued for average periods of seven days in mild and moderate dysentery infections, 12 days in severe infections, 6 to 9 days in acute enteritis and 7·5 and 8·5 days in contact and convalescent carriers. The drug was discontinued when one negative stool culture had been obtained, and the patient was discharged after three further consecutive negative examinations. In this series, there were 34 carriers and two clinical relapses among

280 treated cases of dysentery, 13 carriers and four relapses among 200 treated cases of acute enteritis, 25 carriers and four relapses among 120 cases of enteritis treated symptomatically, and eight persistent carriers among 245 treated contact and convalescent carriers. There were no drug reactions.

In the second group, 3·5 gm. of sulphaguanidine was given to all acute cases on admission, followed by 12 gm. daily until stools were fewer than five per day and then 9 gm. daily. Drug was continued for average periods of 15 to 17 days in the dysentery cases, for 14 to 19 days in the enteritis cases and for 8·7 days in doses of 9 gm. daily in the contact carriers. Treatment was discontinued after three consecutive negative stool cultures and the patient was discharged after three more successive negative examinations. The higher dosage and the longer period of treatment resulted in no carriers or relapses among 69 cases of dysentery, no carrier and one relapse among 80 cases of enteritis, and two persistent carriers among 91 contact carriers. There were two instances of drug-reaction in this group; one a drug rash with fever after eight days' therapy, the other drug-fever after six days' therapy. The authors stress the importance of the dysentery carrier and state that "frequent stool examination of food handlers, follow-up stool studies of discharged hospital cases, and the examination of all troops arriving at and leaving this command were excellent concomitants of good sanitation in preventing bacillary dysentery. In the control of the carrier state, these methods reduced the rate from 11 per cent. to less than 0·3 per cent." *Robert Cruickshank.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

OSBURN, H. S. **Amoebiasis in Infancy.** *Clin. Proc.* Cape Town. 1944, Oct., v. 3, No. 8, 405–12, 3 figs. [10 refs.]

Amoebiasis is by no means unknown in infancy. HOWELL and KNOLL [this *Bulletin*, 1941, v. 38, 267] found 18 cases in 11 years in ages ranging from 8 months to 13 years.

BECKER [this *Bulletin*, 1937, v. 34, 950], in analysis of post-mortem material at Johannesburg, found amoebic infection more or less evenly spaced throughout the age-groups in the Bantu, whilst in the Europeans no cases were discovered among 64 autopsies in the first 20 years of life; Becker, however, admits that his numbers are probably too small for conclusions to be significant. In 21 native patients in the Salisbury and Charter districts of S. Rhodesia, with active *E. histolytica* in the faeces, Osburn found that three were under five years and one of these was under two years of age. An autopsy on another female child under two years revealed amoebic ulceration of the large intestine and numerous amoebic abscesses of the liver. This contained four large abscesses in the right lobe, varying in size from that of a golf ball to a tangerine orange and in addition there were very numerous miliary lesions [the figure shows also a fifth large abscess]. Each of the larger lesions was surrounded by a broad haemorrhagic zone in places half an inch wide. Three were adherent to the parietal peritoneum and were ruptured in removing the liver. The most anterior in the right lobe was adherent to the transverse colon. The walls were shaggy and necrotic. Typical amoebic ulcers were present in the large intestine, tending to coalesce in the caecum, but discrete in ascending and transverse colons. In the upper colon the faeces were dark yellow, but not dysenteric in character.

Although the autopsy was performed after a lapse of 20 hours, the pus taken from a scraping just within the yellow necrotic margin of an abscess revealed

amoebae, which contained red cells and were still motile [illustrated by serial drawings to demonstrate protrusion of pseudopodia]. Numerous forms of *E. histolytica* were present in the walls of the abscesses on section, as well as in the caecum and terminal ileum, together with well-marked lymphocytic infiltration and moderate numbers of endothelial cells.

The author emphasizes the rarity of hepatic amoebiasis in the female, for out of 28 other cases collected by him in Zulus and Rhodesian natives, all were in males. The large number of abscesses present was also remarkable.

It is suggested that further investigation might reveal that this occurrence is not quite so exceptional as might at first sight appear, for in the Enkeldoorn Hospital between September 1942 and May 1944 there were admitted five cases of amoebiasis in children to eleven cases in adults—a ratio suggesting a distribution of infection very different from that usually reported.

P. Manson-Bahr.

PARRY, E. **Intussusception complicating Amoebic Dysentery.** *Lancet.* 1945, Jan. 13, 50.

PAL, J. C. MUKERJI, B., GUPTA, J. C. & CHATTERJEE, M. L. **The Quality of Indian-Made Synthetic Drugs. II. Examination of Iodochlorhydroxyquinoline (Enterovioform) of Indian Manufacture.** *Indian Med. Gaz.* 1944, Oct., v. 79, No. 10, 469–71.

"Indian-made iodochlorhydroxyquinoline differs slightly in chlorine content from the standard product of the same name in N.N.R. 1941, but agrees closely in melting-point, physical characteristics, solubility, iodine and chlorine percentages with the 'Ciba' brand 'Enterovioform.' Its toxicity (one brand only tested) is within safe limits in therapeutic dosages. In clinical trials in controlled cases of amoebiasis in hospitalized patients, it has given comparable satisfactory results.

"The Indian-made synthetic product is therefore likely to be of the proper standard, and wider clinical trial to these brands can be given by the Indian medical profession in suitable cases without any risk to their patients when employed in therapeutic doses."

SHIH LU CHANG. **Destruction of Micro-Organisms.** *J. Amer. Water Works Ass.* 1944, Nov., v. 36, No. 11, 1192–207, 17 figs. on 1 pl. [23 refs.]

The author has shown previously [CHANG and FAIR, this *Bulletin*, 1942, v. 39, 313] that by using a solution of ortho-tolidine [for concentrations of chlorine below 2 p.p.m.], penetration of chlorine into cysts of *E. histolytica* could be demonstrated when the cyst had been exposed to large doses of chlorine as gaseous chlorine and H.T.H. (high test hypochlorite) or chloramines at *p*H 5·0. This penetration of chlorine increased with increase in the chlorine dosages and the contact periods as judged by the greater intensity of the yellow coloration of the cysts. It was also shown that the cyst-penetrating power of chloramines was much weaker than that of gaseous chlorine and H.T.H. Furthermore, associated with this penetration, changes of destructive character were observed in the nuclei within the cysts and it seemed probable that the death of cysts, following exposure to chlorine, was the result of these cytological changes. In the study reported in the present paper more extensive tests were made in an attempt to answer a number of questions:—(*a*) Do different chlorine and chloramine compounds differ in their penetrating power? (*b*) Is there a parallel between the cysticidal power and the penetrating power? (*c*) How do the *p*H and the contact period affect the penetrating power?

(*d*) Does the supposed "nascent oxygen" liberated by HOCl play any significant part in the destructive process? (*e*) Is destruction or poisoning the actual cause of death?

Tests were carried out by adding five drops of a cyst suspension (containing 10,000 to 50,000 cysts) to 40 cc. of various solutions of chlorine and chloramine compounds (at desired concentrations of chlorine and *p*H values) which had been allowed to stand for four hours till Cl_2, HOCl, OCl–, $NHCl_2$ and NH_2Cl and hydrolysis products of organic chloramine compounds, if any, had reached equilibrium. After the desired contact period, the sediment in each tube was washed by centrifugation with distilled water, taken up in 5 cc. distilled water to which a few drops of ortho-tolidine solution was added. Excess of the yellow liquid was washed away by distilled water, and the centrifuged deposit submitted to microscopic examination for degrees of yellow coloration of the cysts. The viability of cysts after exposure to the cysticidal agents was tested by washing them and inoculating them to liver infusion agar medium, while cytological changes were studied by making films on slides smeared with egg albumin, fixing on Schaudinn's fluid and staining with iron haematoxylin.

As a result of these investigations it was found that when cysts were exposed to solutions of gaseous chlorine, H.T.H., dichloramine, monochloramine, Halazone and succinchlorimide, penetration of chlorine occurred. The penetrating power was in the order Cl_2, HOCl, Halazone, dichloramine, succinchlorimide and monochloramine. The greater the concentration of titratable chlorine and the longer the contact period the greater was the penetration. The effect of *p*H on the penetrating power of gaseous chlorine was due to the formation of Cl_2, HOCl and OCl–, the quantities of which increased in this order as the *p*H rose from 2·0 to 8·5. The *p*H effect on chloramines was due to the formation of di- and mono-chloramine. In the case of Halazone it seemed to be due to the hydrolysis product HOCl. The effect on succinchlorimide was not significant. The good penetrating power of Halazone and dichloramine was attributed to the hydrolysis product HOCl. Succinchlorimide and monochloramine were not hydrolysed. The penetrating power of these agents was parallel to their cysticidal efficiency. Hypochlorite (OCl–) was found to be non-penetrating and non-cysticidal. It was thought that the action of chlorine and chloramine compounds was attributable to the active chlorine oxidizing or chlorinating the proteins. It was unlikely that nascent oxygen liberated by HOCl played any part in the process. Definite destructive changes in the cysts, illustrated in a series of microphotographs, occur after exposure to minimal doses of chlorine. It would seem that these changes render the cyst non-viable before oxidation of the proteins, or chlorination of these to form chloramine, which would poison the cysts, can take place. *C. M. Wenyon.*

WELCH, P. B. **Giardiasis with Unusual Findings.** *Gastroenterology.* 1944, Aug., v. 3, No. 2, 98–102.

In a previous paper (*Amer. J. Digest. Dis.*, 1943, v. 10, 52) the author reported upon 13 cases of giardiasis in which radiological evidence was obtained of functional or anatomical changes in the duodenum, duodenal cap, pylorus and prepyloric area of the stomach. Examination of the blood in 12 of the cases revealed an eosinophilia in 58 per cent. After atabrine [mepacrine] therapy six of the cases showing eosinophilia were re-examined and in five the condition no longer existed. In the present paper an account is given of 16 further cases, eight in adults and eight in children—giving a total of 29 cases in the two series. Radiological evidence of functional or anatomical changes was found in three-fourths of all the cases and leads to the suggestion that alterations in the peptic area are characteristic of severe giardia infection. Furthermore,

in 22 of the 29 cases there was an eosinophilia varying from 4 to 13 per cent. In 16 of 21 of these eosinophilic cases there was a return to normal after atabrine therapy. In 15 cases there was a leucocytosis (10,000 or over). In all of these a drop occurred after atabrine treatment. *C. M. Wenyon.*

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

BULMER, E. **Weil's Disease in Normandy: its Treatment with Penicillin.** *Brit. Med. J.* 1945, Jan. 27, 113–14.

During the present campaign in North-West Europe sporadic cases of Weil's disease have so far (Dec., 1944) been met with only in Normandy. They all occurred from the middle of July to the end of September, during which period the author had been informed of 39 cases. However, since all except two of these patients showed well developed jaundice, it is probable that many cases were missed and the author estimates that about 100 cases may have occurred.

Spirochaetes were found in the blood in several instances and often in the urine. In most cases positive agglutination tests were obtained by sending the blood to the U.K. Sixteen of the patients were treated with penicillin, 40,000 units three-hourly, the average total amount given being about 1,125,000 units. The treatment seemed to shorten the duration of the fever and to reduce the number of relapses; also, there was a very general clinical impression that the treated patients improved dramatically within 36 hours. On the other hand, penicillin did not seem to influence the degree and duration of cholaemia, nor to affect the rate of disappearance of icterus from the skin or of bile from the urine. It also did not affect the degree of nitrogen retention or the rate of disappearance of albuminuria.

One out of the 16 treated patients died of uraemia; two out of 23 untreated patients died, one of myocarditis and the other of uraemia.

The author considers that further work on the treatment of Weil's disease with penicillin is desirable; it seems essential to give the treatment early, and the dosage should be high. *E. Hindle.*

CARRAGHER, A. E. **A Case of Weil's Disease treated with Penicillin.** [Memoranda.] *Brit. Med. J.* 1945, Jan. 27, 119.

The history of a soldier invalided from France with pyrexia of six days' duration who reached a hospital in Wales, on September 12th, 1944. He stated that during August he had bathed frequently in a rat infested river in Normandy. Spirochaetes were found both in the blood and urine and the patient's serum agglutinated *L. icterohaemorrhagiae* to a titre of 1 : 1600.

Penicillin therapy was started with 20,000 units intramuscularly three-hourly for four days and then four-hourly for another three days, the total dosage being 900,000 units. The condition of the patient improved markedly within a few hours and spirochaetes disappeared from the blood and urine within 15 hours of the first injection. The patient did not develop an after-fever, and was discharged perfectly well within 17 days. *E. Hindle.*

AUGUSTINE, D. L., WEINMAN, D. & MCALLISTER, Joan. **Penicillin Sodium Therapy in Experimental Weil's Disease.** *New England J. of Med.* 1944, Sept. 7, v. 231, No. 10, 358–9.

The authors used a strain of *Leptospira icterohaemorrhagiae* which was very virulent for guineapigs, killing them within seven days. Two experiments

were made. In the first experiment, 10 guineapigs, each 180 gm. in weight, were inoculated with the spirochaetes and showed jaundice on the fourth day; five were then injected intraperitoneally with 4,000 Oxford units of penicillin sodium in 1 cc. of saline every four hours for 78 hours or until death occurred, while the other five were kept as controls. Of the treated guineapigs, one died after 4,000 units, two after 8,000, and the remaining two died on the morning after the final injection (total 48,000 units). The controls died before the last two of the treated animals did. At autopsy, all the animals showed similar characteristic lesions, with motile leptospirae in the liver and kidneys.

In the second experiment, eight guineapigs were similarly infected, but the treatment of four was begun 38 hours after inoculation, and each was given 5,000 units of penicillin sodium intraperitoneally every four hours for 48 hours (total 60,000 units). Of the controls, one died on the third day, and two on the seventh day, and showed lesions of Weil's disease at autopsy; the fourth guineapig recovered and was killed on the 15th day after inoculation, the organs being apparently normal. None of the treated guineapigs showed jaundice or other signs of illness except roughness of fur; one was found dead on the fourth day after completion of treatment, another on the fifth day, and a third on the seventh day. At autopsy leptospirae were found in the liver and kidneys but there were no severe lesions. The last guineapig was killed while in apparently good health on the 11th day after treatment (15th after inoculation); the organs appeared to be normal and no spirochaetes were seen.

Penicillin, therefore, seemed to have some suppressive effect but was not curative. The results differ from those of HEILMAN and HERRELL [this *Bulletin*, 1944, v. 41, 758]; they, however, used a strain of leptospira of low virulence and gave penicillin 12–24 hours after inoculation. *J. F. Corson.*

AFRIQUE OCCIDENTALE FRANÇAISE: RAPPORT SUR LE FONCTIONNEMENT TECHNIQUE DE L'INSTITUT PASTEUR EN 1942 [DURIEUX, C.]. pp. 81–4. **Étude d'un spirochétidé isolé du sang de l'homme au cours d'une maladie fébrile. [The Study of a Spirochaete isolated from Human Blood during a Febrile Attack.]**

An African child showed a temperature of 39·5 to 40°C., which lasted for 15 days, accompanied by slight clinical symptoms including enlarged liver and headache, after which the patient recovered. There were no signs of jaundice. Leptospiral organisms were isolated from blood collected on the fifth day of the disease, by means of culture in ordinary broth. Attempts to infect guineapigs, rabbits, rats and mice were negative, but two inoculated monkeys, *Cercopithecus patas*, showed signs of infection. One died after 22 days and, although the autopsy was negative, leptospirae were recovered by blood culture. The second monkey showed vague symptoms including loss of appetite, and was accidentally killed after 26 days. Leptospirae were also recovered by culture of heart blood.

It is considered that this may be another leptospiral infection related to mud fever. *E. Hindle.*

YAWS.

FINDLAY, G. M., HILL, K. R. & MACPHERSON, A. **Penicillin in Yaws and Tropical Ulcer.** [Correspondence.] *Nature.* 1944, Dec. 23, 795–6.

Penicillin was found to be effective in a trial, in the Gold Coast, in 24 cases of yaws in children and 25 cases of tropical ulcer.

Yaws.—Two cases were primary, 22 secondary; the patients were given 50,000-100,000 Oxford Units of penicillin intramuscularly during 12–24 hours. "The results were dramatic and nineteen cases were clinically cured in an average time of 6½ days." The two cases of primary yaws were cured completely, with reversal of the result in the Kahn test, within seven days; in the cases of secondary yaws, the "snuffles" disappeared, the papules desquamated, and the yaws dried up within 24 hours, and in 2–10 days, only scars remained. In a case with severe bismuth stomatitis, penicillin cured both the yaws and the stomatitis within 48 hours. There have been no toxic results. In two cases of secondary yaws, observed for six weeks, the result of the Kahn test was not reversed, but the authors think that larger doses—500,000–1,000,000—would produce reversal.

Tropical ulcer.—Many of the ulcers were several months old; they were treated by the injection of 100,000 Oxford Units in 24 hours and the application of penicillin ointment (250 units per gm.); in some cases the local application only was used. Great improvement took place within 24 hours; granulations filled the base of the ulcer, and epithelialization began at the edges. Within a few days the ulcers became practically sterile.

Cancrum oris.—Two severe cases in children were greatly improved and one recovered. *J. F. Corson.*

LEPROSY.

British Empire Leprosy Relief Association (Madras Provincial Council). **Annual Report 1943–44** [Austin, T., Chairman, Executive Committee]. 20 pp. 1944. Madras: Diocesan Press.

This report appears to have been written by the Hon. Secretary, Dr. R. G. Cochrane, and deals in part with the same matter as in the following paper by him. The main facts recorded will be dealt with under this heading and the general considerations under the following paper.

An advance is reported in an order for the admission of cases of leprosy to general hospitals and in arrangements for the instruction of the students of Madras Medical Colleges by an expert on leprosy. Epidemiological enquiries have been continued through village surveys, regarding which statistics are recorded to show a gross incidence of 24·7 per mille and a child rate of 26·8 per mille; very high rates. The open case rate was only 11·5 per mille in an area with poor economic conditions. Repeated surveys confirm the earlier conclusion that abortive lesions have a great significance. In the development of lepromatous cases, incipient lesions of childhood in the form of simple macules, including neural macules, play an important part and may be classed as prelepromatous in nature. The night segregation of infective cases in villages, to lessen their contact with susceptible children, has been followed by a reduction in child infections. It is proposed to examine all school children in Madras City for signs of early disease and to allow contacts to be traced, but a leprosy hospital to hold 500 infective cases is urgently needed. Uninfective crippled beggars could be provided for by a religious body. It is estimated that in Madras city there are 5,000 to 7,000 cases; of these at least 500 to 750 are probably infective. A children's Leprosy Sanatorium at Ettapur admitted

31 boys during 1942, discharged 17 and had 39 remaining at the end of the year. Such institutions should be multiplied. Surveys show very great variations in incidence (from nil to 124 per mille) in villages close to each other; there is much greater contact with infective patients in some villages than in others. In an anti-leprosy campaign, highly infected villages should be sought out and dealt with. As elsewhere, lepromatous cases gave negative lepromin reactions. Work on the Wassermann reaction showed increasing positive results with the advance of lepromatous cases without any indications or history of infection with syphilis; these were, consequently, the direct result of leprosy infection. *L. Rogers.*

COCHRANE, R. G. **Leprosy Control with particular reference to the Madras Presidency.** *Indian Med. Gaz.* 1944, Sept., v. 79, No. 9, 438–45.

The author discusses the present position and needs of leprosy control in India in the light of his last eight years' investigations in Madras. He first endorses the recommendation of the Manila Leprosy Conference of 1931 to drop the word "leper" from the medical vocabulary. He believes that with adequate finance and personnel the disease can be controlled, but out-patient treatment alone is not sufficient, though even in lepromatous cases early and intensive treatment gives a good chance of recovery. He discusses anti-leprosy work under a number of headings. Leprosy institutions are required in all districts in which surveys reveal serious prevalence of the disease, to provide both segregation and treatment of "open" (that is infective) cases. In addition to the large Lady Willingdon Leprosarium at Chingleput, five smaller institutions under the Mission to Lepers require to be modernized and enlarged, each to accommodate 400 cases under two doctors, with agricultural and industrial occupation. Courses of instruction on leprosy to medical practitioners should be longer than fourteen days, as at present. Surveys on the lines long ago introduced by MUIR [*Leprosy in India*, 1931, v. 3, 50] are essential to enable the seriously infected areas to be located and dealt with. Rural units should be established where required, together with village or family segregation. Among the 90 per cent. of the population engaged in the day time in agriculture night segregation of infected cases may do much to lessen the danger to children. For urban conditions he advocates either isolation in an institution, or home isolation with a separate room, bedding, cooking utensils, etc., but admits the difficulties in enforcing such regulations, and that this is only possible in the case of those with sufficient means. All municipalities should therefore provide an institution for infective cases. In no other way can the problem be solved, and the sooner this is realized and provided for, the quicker will leprosy be controlled. Special sanatoria for children are also advised, because they cannot be isolated at home. The child contacts of infective cases should be examined periodically for early symptoms. Deformed and derelict cases and beggars should be provided for by philanthropic institutions. Propaganda must be continued to educate public opinion. The Madras Public Health Act is being modified to bring it up to date and to compel the infective patients to isolate themselves or to submit to compulsory segregation. At present no distinction is made between open and closed cases. Facilities for segregation will have to be provided, but compulsory measures should be used only in cases of emergency. No success can be expected unless a well qualified medical officer is placed in charge of the campaign in each province. *L. Rogers.*

LEPROSY IN INDIA. 1944, July, v. 16, No. 3, 109–13. **The Annual Report for 1943 of the Indian Council of B.E.L.R.A.**

PRETORIA LEPER INSTITUTION. **Minutes and Papers of a Conference on Leprosy held at Pretoria Leper Institution on 18th & 19th September, 1944.** 51 typed pp. & 1 folding chart.

This important South African leprosy conference was attended by the members of the Leprosy Board and medical officers from the institutions of South Africa, Basutoland and Southern Rhodesia, and the papers dealt with below were read. The following are the more important recommendations :— The occurrence of relapses in probationally discharged cases should be further investigated, together with the tests made before the discharge of patients. Better control of those discharged should be carried out by periodical examinations by a leprologist. District surgeons should be induced to revise their knowledge of leprosy by further courses of instruction to enable them to recognize the signs of recrudescence of the disease. The question of Native inspectors should be investigated. University instruction on leprosy should be given with the aid of coloured films and photographs. Demonstrations of methods of treatment, etc., were also given by members present. The question of home segregation was discussed and objections were raised to this being allowed in cases positive bacteriologically, on the ground that it was impossible to ensure that the regulations were always faithfully carried out. Brief discussion took place on some of the following papers which were read at the meetings.

Some of the Problems of Leprosy was the title of a paper by Dr. F. S. DREWE of the Mkambati Leper Institution, where he had worked for 25 years. He points out that we have no certain knowledge regarding the mode of entry of the *M. leprae* into the human system, and suggests the tonsils as a possible site, although he has never found the organism in smears from them. He next discusses types of leprosy in relation to the resisting powers of the infected, quoting from various writers. He suggests that the early lesion consists of a small-cell infiltration which might later progress to either tuberculoid or lepromatous changes. Drewe mentions the observation of Dr. Fox of the South African Institute for Medical Research that the diet of natives of the Transkei is seriously deficient in calcium, and thinks that this might influence their resisting powers. He states that in some cases all lepromatous nodules disappear during the two or three days before death from tuberculosis. He advocates a period of complete rest, good food and fresh air, for leprosy patients on the lines of sanatorium treatment of pulmonary tuberculosis in order to increase their resistance. Good results are obtained from injections of up to 14 cc. of ethyl esters by infiltration at the base of the nodule rather than by injections of small doses into them. Neural macules respond to intradermal injections. He has not found the sedimentation test of much prognostic value, but the lepromin test is more reliable.

Criteria of Cure by A. R. DAVISON, Pretoria Leper Institution.

The occurrence of reactions in 12 of 15 probationally discharged patients who had been detained on humanitarian grounds raised the question of the standard of cure or arrest, which has never been definitely laid down. The present custom is to require 12 negative smears at monthly intervals except in the case of a new admission in an obviously burnt-out stage. Further, the patient must show no raised or red macules and no new ones. A case is considered to be clinically reactive, if, after a period of quiescence, new lesions break out or old ones become raised or red. A survey of probationally discharged cases is being arranged, but only nine local cases have yet been examined, one of which was reactive. Hitherto, all discharged patients are examined by a district surgeon every six months for the first three years and every 12 months for three years more. Davison found 12 of 38 discharged cases in one district to be recrudescent, but all of them were ill-housed, ill-clothed and ill-fed. He therefore advises that

before discharge, patients with nerve leprosy should be free from all activity for 12 months, and that in those previously bacteriologically positive, 24 monthly smears should be negative, including at least eight skin smears, and X-rays should show no dead bone. Further, the examinations by the district surgeons should be made every three months, and the patients' discharge chart should be sent to them instead of being pigeonholed by the magistrate, as at present; the district surgeons should have a good knowledge of leprosy. Each case, however, should be examined by a leprologist once a year.

Leper Institutions by A. R. Davison.

The author deals with the planning of a leper institution in a country with the fairly low incidence of 1 to 2 per mille and "with no stinting of the money necessary to bring the policy to a successful conclusion." [South Africa and the Southern U.S.A. are probably about the only leprosy-infected countries which fulfil those conditions.] He considers that the sparseness of the population and the conflict with the South African policy of segregation make out-patient treatment centres unsuitable. He also objects to leper villages on account of the infertility of the soil, which would necessitate immense tracts of country being set aside if the patients are to subsist on its produce. This leaves only leper settlements with attached hospitals, preferably to deal with a minimum of 1,000 patients so as to allow of two or more doctors being employed, one of whom should be a research worker. The lay staff should include a gardener-farm-manager. The site should be within 10 miles of a town, and smallholdings should be allotted to patients and their produce bought by the institution. Segregation of the sexes is essential. The superintendent should have magisterial powers, but native courts should try most offences. Committees of the patients should be formed and general meetings held each year to discuss policy and procedure. The families of breadwinning patients should receive maintenance grants.

Compulory Segregation by A. R. Davison.

The author begins with quotations from medical literature in support of his belief that, although under normal conditions leprosy has a low degree of infectivity, yet under conditions of poverty and malnutrition, as in Nauru Islands, "the degree can assume almost epidemic proportions." He goes on to say that the only argument against segregation is its expense. On the importance of segregation he quotes from the Leprosy Commission of the League of Nations, which states that "it may be administratively possible and advisable to make it compulsory," and from the Cairo Congress on the methods of isolation of open cases in institutions, villages or in the patients' homes; the last is the least effective. He considers that the conditions in South Africa are by no means unfavourable for the spread of leprosy, and holds that the conditions would be worse today if there were no segregation. Since 1916 the European cases have declined from 198 to 74; the Cape Coloured cases numbered 345 in 1913 and are 120 today. The decline among the natives is less but it is certain that cases among them are now being seen in an earlier stage. The average duration of the disease prior to admission used to be about nine years; today it is nearer two years. He agrees that in countries with large numbers of leprosy cases compulsory isolation in institutions "is out of the question because the expense would be out of all proportion to the financial resources." South Africa is one of very few countries that can afford to carry out a policy of compulsory isolation for all stages and types of the disease, and he concludes that by its means the disease is being controlled, if not stamped out, and that any relaxations of that policy could lead to an alarming increase of the disease. [Not long ago the cost of compulsory isolation in South Africa was a little over £50 per head.]

Conjugal Infections in Leprosy is the subject of a short note by B. MOISER of Southern Rhodesia. The rate of conjugal infection in 700 of his cases is only 1·57 per cent. [a much lower figure than that given by ROGERS in *Leprosy*]. In his institution he advises that married couples should not be separated when only one is infected. He suggests that the low rate of infection in such couples may be related to sex hormones, which should be investigated in the hope of being able to make use of sex hormones prepared from leprous patients in treatment.

In his paper *The Transmission of Leprosy* MOISER reports that 69 per cent. of cockroaches at Ngomahuru, caught in the hospital grounds or in kraals in the Native Reserve, show in their gut or faeces acid-fast oval bodies, which, he thinks, are worthy of investigation in view of the number of leprosy infections he has seen, in which family or other contact could not be traced.

The Campaign against Leprosy in Transkei, by P. A. THORNTON.

This paper deals with leprosy work at the Emjanyana Leper Institution, South Africa, and the author attempts to estimate the value of the leprosy Campaign carried out during the last ten years in Transkei, which has an estimated population of a million and a half. The author opens with a statement that in the previous month 569 patients with active leprosy were seen by the medical board, and that 146 had been recommended for discharge. During the previous five years there had been an average annual admission of 37 fewer cases than in the previous five years, but the decrease may be due to the fact that there are now fewer practitioners, doubtless because of war demands. During the last ten years 27·3 per cent. of all patients had been discharged; all were neural cases, which form just over half the numbers in the institution. There has been some increase in recrudescences, but not an alarming one, with readmissions after an average of about three years, but very few were positive for bacteria and many of them came for surgical treatment. The methods of surveillance of discharged patients needs revision. He concludes that the campaign is apparently meeting with a small degree of success and that methods of treatment at present used are fairly successful.

Emjanyana Leper Institution.

Period 1935 *to* 1944.

	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944
Admitted for first time	160	217	207	256	174	210	181	172	131	145
Numbers seen by Board	598	601	649	663	634	670	608	600	543	569
Discharged as Arrested	114	146	193	208	203	144	249	138	181	146
Percentage of Discharges	12·5	24·3	30·1	31·5	30·7	21·5	40·9	23	33·3	25·6
Recrudesced Cases...	18	8	4	13	12	31	26	23	30	35
Death	70	79	54	87	64	43	59	69	55	71

L. Rogers.

AUSTIN, C. J. **Central Leper Hospital, Makogai (Annual Report for 1943).** *Fiji, Legislative Council. Council Paper No. 17.* 1944, 7–9.

In 1943 the number of patients at the beginning of the year was 645, the admissions numbered 77, the discharges 65, 26 died and 631 remained at the end of the year, a reduction of 14. Of a total of 942 patients admitted in ten

years, 295 came from Pacific Islands beyond the Colony of Fiji; in the same period 75 were readmitted, 17 of whom were again discharged. Of the 77 admitted during 1943, 17 were Fijians, 20 Indians, 32 Cook Islanders, 5 Samoans, 2 Niue Islanders and 1 Euronesian. Of the 32 Cook Islanders no less than 24 were early Neural-1 cases, so it is not surprising that a high proportion of those discharged were persons from those islands. Of 64 conditionally discharged, 52 were Neural-1 and Neural-2, four were Lepromatous-1 and eight Lepromatous-2 cases, and one formerly discharged lepromatous case was readmitted with retrogression. Among the Cook Island cases there were far more who were relatives of other lepers than among other communities, and many of them were children, so, without care, the disease would soon assume a far more threatening aspect. An important feature of this institution is the amount of paid work the inmates do both in agriculture and handicrafts, for their earnings amounted to £2,890 in the year. A Fiji branch of the Lepers' Trust Board has also been formed to assist those in need. Progress is thus being made in many ways in this up-to-date institution under the care of Dr. Austin. *L. Rogers.*

DEGOTTE, J. Contagiosité de la lèpre neurale. Enquête épidémiologique chez les Pygmées. [**Infectivity of Neural Leprosy: Epidemiological Study among the Pygmies.**] *Rec. Travaux Sci. Med. Congo Belge.* Léopoldville. 1944, Jan., No. 2, 162–4.

This short note on leprosy prevalence among the pygmy tribes of the Belgian Congo raises the question as to how far neural types of leprosy may be contagious to the healthy. The author's experience has led him to admit the occurrence of new infections in areas with only neural cases or with only vague evidence of the presence of lepromatous patients. He admits that he is dependent on the accuracy of his informants, but the examination of a number of pygmies confirmed his hypothesis and he gives data of a number of villages in which only neural cases were found, mostly of a very mild type. He points out that nerve cases may at times show lepra bacilli in their nasal cavities, which are likely to be infective. In the Nepoko area, 5 to 6 per cent. of the population are infected and out-patient treatment is the method of choice for most cases, but those with lepra bacilli in the nasal secretions are better isolated. *L. Rogers.*

DAVISON, A. R. **Decolorizing of** *Mycobacterium leprae.* *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 49–51.

In nerve leprosy, incision and scraping of the perineurium of thickened nerves almost invariably reveals bacilli, a scraping of the nasal mucosa may do so, but an incision of a macule rarely does. In 80 per cent. of these cases lepra bacilli are not found, and diagnosis must therefore be made without by other means. The laboratory technique for staining is not standardized, and presents pitfalls. The author has found inadequate the recommended method of staining with fuchsin for two minutes, with the same period of time for decolourizing in a 5 per cent. sulphuric acid and for staining with methylene blue. He advises staining for five minutes in warm fuchsin, decolourizing for 20 minutes in 5 per cent. sulphuric acid, and counterstaining for two minutes with methylene blue. Otherwise diphtheroids are liable to be mistaken for Hansen's bacillus. *L. Rogers.*

PARMAKSON, P. Die pathohistologische Reaktion der Haut bei Lepra. [**The Pathological Reaction of the Skin in Leprosy.**] *Deut. Tropenmed. Ztschr.* 1943, Nov. 1, v. 47, No. 21/22, 545–77, 10 figs. [45 refs.]

The author reports the results of a careful study of 20 lepromatous and 18 nerve leprosy cases, in different stages of the disease, by means of microscopic

sections of the affected skin (including examination for *M. leprae*), the sedimentation test and the Mitsuda reaction. The most important data are shown in a table and the answers to five questions he set himself to deal with are as follows :

1. Active skin lesions of nerve leprosy are characterized by tuberculoid changes.
2. In the case of clinically lepromatous lesions the morbid histology shows no tuberculoid changes in the skin.
3. In clinical nerve cases no lepromatous changes are found on section.
4. Tuberculoid and lepromatous changes do not appear simultaneously.
5. It is improbable that a change from one type to the other could be followed histologically. The typical changes of one type disappear before those of another type appear.

The data recorded regarding the red cell sedimentation rate are in accordance with those of other observers in that it is increased in well-marked lepromatous cases, although this may not be so in early cases. Nerve cases show increased rates only when complications are present, such as perforating ulcer of the foot. The Mitsuda reaction was negative in nearly all lepromatous cases except those in a very early stage, and positive in nerve cases, as found by others. [The histological changes are well illustrated and the paper is worthy of close study by those interested.] *L. Rogers.*

SLOAN, N. R. **Early Diagnosis of Leprosy, as seen in Hawaii.** *Hawaii Med. J.* 1944, Jan.–Feb., v. 3, No. 3, 111–20, 4 figs.

The first part of this paper deals with the subject generally and the author is in agreement with medical opinion regarding transmission, and race, sex and age incidence. He commences by claiming that compulsory segregation is effective in Hawaii, and that the decline in known active lepers from 1,175 in 1890 to 390 in 1943 is evidence of this. A careful analysis is given of the symptoms in 743 cases, which shows the following frequency of the more common symptoms :—Macules (spots and blotches) 344, nodules 97, anaesthesia 64, ulcers 63, swelling of skin 44, muscular weakness 31, contracture of fingers 28, erythema 17, etc. The early symptoms are then described on the usual lines and the methods of examination given. These will be useful to those without much experience of the disease. *L. Rogers.*

PEIXOTO, P. G. **Leprosy and Syphilis.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 43–8, 6 figs on 2 pls.

This is the report of a case in which the diagnosis between leprosy and syphilis was difficult ; the patient was a negress in Brazil, who had never lived with a leprosy patient and denied having had syphilis. A number of somewhat infiltrated, lighter-coloured patches were present on the face, body and limbs with some loss of sensation to heat and pain, but not to touch ; there was no thickening of nerves. No lepra bacilli were found in the nose or in a gland. The histamine test showed lack of the second erythema on all the lesions and, microscopically, the giant cells of Langhans were found in a few places. Wassermann and Müller blood tests were positive and neoarsphenamine treatment produced considerable improvement in the skin lesions, without modifying the loss of sensitivity. It was therefore concluded that the case was one of mixed leprous and syphilitic origin. *L. Rogers.*

FERNANDEZ, J. M. M. **Sensitization to Lepromin in presumably Non-Leprous Individuals.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 15–22. [12 refs.]

After reference to the late reaction produced by Mitsuda's method, which is here called integral lepromin, and the early reaction induced by injection of the protein fraction of *M. leprae*, the writer reports the results of his studies of the sensitizing action of integral lepromin and of suspensions, in mineral oil, of Hansen's bacilli killed by heat, of the tubercle bacillus killed by heat, and of the typhoid bacillus. He reports that presumably non-leprous subjects can be sensitized to lepromin by intradermal injection of an oily or aqueous suspension of *M. leprae* killed by heat, and by suspensions of killed tubercle bacilli. He also found the early lepromin reaction to be attributable to previous sensitization induced by either lepra or tubercle bacilli. On the other hand, sensitization to lepromin was not induced by previous intradermal injection of purified lepromin protein (L.P.P.) or of suspensions of killed typhoid bacilli. The duration of sensitivity to lepromin is not yet established, but it has persisted as long as five years after intradermal injections of integral lepromin. It has not yet proved possible to provoke a supposedly protective allergy, since it is apparently dependent on an unknown factor which may be constitutional.

L. Rogers.

ROSS, Hilary. **Euglobulin in Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 23–6. [10 refs.]

Estimation of the total proteins, albumin, globulin and euglobulin have been made in 150 cases of leprosy of various types and stages. The methods used are described and the euglobulin-tyrosin indices are given. In 147 cases the index was above normal, and of these the albumin-globulin ratio was below normal in 123, and in the rest it was normal. Higher tyrosin indices were met with in active and moderately or far advanced cases. It is suggested that hepatic dysfunction and liver damage may be the aetiological factor in the changes noted.

L. Rogers.

ECCLES, C. G. & ROSS, Hilary. **The Mazzini Flocculation Slide Test compared with the Kolmer-Wassermann and Kahn Standard Tests in Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 27–31, 3 figs.

The authors refer to the results obtained by MAZZINI [see RATCLIFFE, *Bulletin of Hygiene*, 1940, v. 15, 716] with his flocculation slide test with the serum of 60 leprous donors, referred to at the Washington Serology Conference of 1941 [*ibid.*, 1942, v. 17, 849]. Of these only 17·2 per cent. were positive against 54·2 per cent. with Kolmer's simplified complement fixation test and 59·6 per cent. with the Kahn standard test. The Mazzini test has the advantages of economy of time and materials and ease of preparing the reagents. The present authors record results on 142 sera in which there were fewer positive results with the Mazzini test (with 28·9 per cent.) than with the Kolmer and Kahn tests (33·8 and 39·4 per cent., respectively), but the Mazzini test showed 16·9 per cent. doubtful reactions against 11·2 and 4·4 per cent. with the other two tests respectively. On account of its greater simplicity the Mazzini test should be of special value for use in mobile laboratories and in small or isolated leprosaria.

L. Rogers.

FAGET, G. H. & POGGE, R. C. **Pooled Blood Plasma Transfusions in the Treatment of Leprosy.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 32–5.

Although certain forms of serum treatment of leprosy have been advocated, the use of normal human serum or plasma has not been given a fair trial in

leprosy. Large supplies of pooled human plasma are now available and are being used in certain infections. Liquid plasma was procured for the trial now reported, it was thought that it might prove of value in the hypoproteinaemia and nephritis of leprosy, even if no specific action was obtained. Twelve patients, six of them in an advanced and nearly hopeless state, volunteered for the trial. Possible improvement was noted in two, unfavourable effects in five, and no evident effects in the remaining five. Two of the three cases in which the prognosis appeared to be most favourable reacted unsatisfactorily, so the results showed no benefit. *L. Rogers.*

CHORINE, V. Le sulfamide dans la lèpre. Traitement des plaies, des brûlures, des ulcères et des maux perforants chez les lépreux. [**The Treatment of Wounds, Burns, Ulcers and Perforating Ulcers, in Leprosy, with Sulphanilamide.**] *Bull. Soc. Path. Exot.* 1943, Jan. 13 & Feb. 10, v. 36, Nos. 1–2, 46–55. [13 refs.]

This paper deals with local applications of para-amino-phenyl-sulphamide [sulphanilamide] in wounds and ulcers of persons with leprosy. Fresh wounds in sufferers from leprosy do as well under this treatment as those in other subjects, and this is also true of surgical wounds, examples of which are given. Burns, which so often occur in anaesthetic subjects, have also given excellent results. Of greater interest is the success of the local treatment with sulphonamides in 18 out of 19 cases of ulcers other than the more obstinate perforating ulcers in neural cases; some of them were of two to three years duration. In these cases the wounds were washed in boiled water and sprinkled or coated with a paste of the preparation; at first daily and, after suppuration had ceased, every two or three days, to act on secondary infection. Healing is sometimes slow in cases with much damaged nerves and perforating ulcers, and applications of silver nitrate may be required in the later stages, but success was obtained in over 50 per cent. of these also. *L. Rogers.*

CHORINE, V. & CHABAUD, A. Lèpre du rat et sulfamide. [**Rat Leprosy and Sulphanilamide.**] *Bull. Soc. Path. Exot.* 1943, Mar. 10 & Apr. 14, v. 36, Nos. 3–4, 82–5.

A former trial reported in 1936 [this *Bulletin*, 1937, v. 34, 319] of the treatment of rat leprosy by para-amino-phenyl-sulphamide [sulphanilamide] in doses of 10 mgm. two or three times a week showed no effect in retarding the progress of the disease. Subsequent trial of this drug in a case of human leprosy showed that the bacillus of Hansen is sensible to the action if sufficiently high doses are injected directly into the diseased tissues, but it is not effective in any feasible oral doses. The present authors have, therefore, repeated their attempts to control the progress of rat leprosy by injections of this drug, which is also known as 1162F, using larger doses than in the former trials. Only slight retardation in the development of the rat disease was obtained. Moreover, no direct lethal action on rat leprosy bacilli was obtained after exposing them to the action of a 2 per cent. saline solution for up to 72 hours. *L. Rogers.*

BURGESS, P. **A World within a World.** *Internat. J. Leprosy.* Cleveland, Ohio. 1943, Dec., v. 11, 1–7.

In this article the President of the Leonard Wood Memorial deals with leprosy as a great social and economic problem with a view to initiating thought toward a practical solution. He proposes a world federation of communities of infected persons, which may become largely self-supporting through employment in manufacturing, farming and animal husbandry, with a common

coinage and transportation. Excessive costs prohibit any appreciable increase above the present 3 per cent. of cases in leprosaria except as almost self-supporting communities, because an annual cost of a few dollars a head for partial support would amount to a staggering sum. If only medical care and spiritual and physical leadership had to be supplied the cost would not be impossible. He estimates the present victims of Hansen's disease (as he prefers to call it) and their dependants at not fewer than 15,000,000 people. The following are some of the problems which require to be dealt with, when considering any form of segregation:—

1. Isolation of the patients from their families is one of the most difficult problems.

2. Families left uncared for through isolation of their head. This includes provision for infants born in a colony and those born before the admission of their parents; for he advises that conjugal partners need not be separated, because the proportion of infections among them is small. The simplest plan is to provide accommodation for the children near their parents, so as to allow of visits.

3. Life in an abnormal community is the most "hideous prospect" for the isolated, who therefore needs to have his family near.

4. Unwillingness to work when deprived of freedom is not entirely without justification, so the entrants to colonies should be volunteers, and they should be attracted by suitable conditions and medical care. Refusal to work should result in removal to a leprosarium without membership of the proposed community.

5. Partial inability to work should be met by expert supervision.

6. Increasing inability to work in advanced cases should not make the patients the subjects of charity but they should be encouraged and helped to provide for their own physical needs, with consequent saving of large sums which could be used for providing doctors, etc. Patients should be paid daily wages. Maimed uninfective patients should be in special colonies.

7. Lack of work because of lack of markets could be overcome by distribution to the proposed world federation of communities.

It is recognized that these are proposals to build a new world, which, if successful should pay generous dividends. Suggestions for its improvement are invited. *L. Rogers.*

HELMINTHIASIS.

ROGERS, W. P. **Studies on the Anthelmintic Activity of Hexylresorcinol and Tetrachlorethylene.** *Parasitology.* 1944, Sept., v. 36, Nos. 1 & 2, 98–109, 9 figs. [26 refs.]

Some of the effects of the physical and chemical properties of the environment of intestinal parasites were investigated by TRIM [this *Bulletin,* 1944, v. 41, 596] who studied the action *in vitro* of bile salts and mucin on the rate of penetration of hexylresorcinol through the cuticle of *Ascaris lumbricoides.* The author sought to supplement Trim's work and to develop a method of checking *in vitro* results by experiments done *in vivo.* For testing techniques hexylresorcinol was used, because, as a result of Trim's work, its mode of action is better known than that of other anthelmintics. Tetrachlorethylene was also used.

The *in vivo* method used was perfusion of the drug through a section of the small intestine of rats infested with *Nippostrongylus muris,* a nematode which is taxonomically allied to the trichostrongyles of sheep which cause much

economic loss and are refractory to treatment. They and *N. muris* live in a similar environment in the small intestine. The apparatus used is figured and described. Mortality of the nematodes was estimated by removing the piece of gut perfused to aerated Tyrode-glucose solution at 38°C., scraping the mucosa with a blunt scalpel and transferring the nematodes, thus set free, to Tyrode-glucose solution saturated with 95 per cent. O_2, 5 per cent. CO_2 gas mixture at 40°C. in a counting dish. After half a minute the proportion of active worms was determined over a period of 4 minutes. The same examination was done after incubation of the parasites in saline for 1 hour. The accuracy of this method was confirmed by killing known numbers of nematodes by heat or 1/1,000 carbon tetrachloride in saline, and mixing these with known numbers of living nematodes incubated in saline for two hours.

The effects of mucus on drug efficiency were studied by examining separately after perfusion the nematodes free in the gut lumen and those which had to be scraped from the mucosa, *i.e.* which were under the mucus. Trim (*loc. cit.*) showed that gastric mucus inhibits the action of hexylresorcinol. Anthelmintics may, by the irritation they cause, induce mucus secretion. The amount of mucus per unit area and unit weight of small intestine before and after perfusion was therefore determined to find out the effect of hexylresorcinol and tetrachlorethylene on mucus secretion. Because perfusion tended to loosen the mucus round the nematodes, the drug penetration observed was probably much better than can be expected under natural conditions. It was found by preliminary perfusions, by X-ray examination of the passage of a barium meal and by experiments on the rate of passage of hexylresorcinol along the alimentary canal, that a perfusion time of 2 hours was the most reasonable.

The effect of anthelmintics was greater on nematodes free in the gut lumen than on those attached to the mucosa. A concentration of 1/2,000 hexylresorcinol was most active in the presence of 0·2 per cent. sodium oleate, probably because of the surface activation caused ; but the soap itself showed a rapidly increasing anthelmintic activity in concentrations above 0·2 per cent. Similarly 1/2,000 hexylresorcinol in the presence of 0·125 per cent. of sodium laurate inactivated 100 per cent. of the nematodes and in the presence of 0·031 per cent. of sodium laurate 90 per cent. were inactivated, probably because the soap itself was anthelmintic, 0·5 per cent. of it killing almost all the nematodes, rendering them almost colourless, with maceration of their tissues. Tetrachlorethylene, on the other hand, was not markedly affected by sodium oleate. The addition of 0·03 per cent. sodium taurocholate increased the anthelmintic action of 1/2,000 hexylresorcinol, 70 per cent. of the nematodes being then inactivated, but decreased it when 0·25 per cent. or higher concentrations of bile salt were used. High concentrations of bile salt removed the gut mucus. Tetrachlorethylene in moderate concentrations was not greatly affected by bile salts. Ascorbic acid had little effect on the action of hexylresorcinol. For the *in vivo* tests of anthelmintic action the egg counts done before treatment were used to predict the number of nematodes expected to be present before dosing. The results showed that 115 mgm./kgm. hexylresorcinol, *i.e.* one-fifth of the L.D. 55 dose (see LAMSON, BROWN and WARD, *J. Pharmacol. & Exper. Therap.*, 1935, v. 53, 568–575), did not apparently affect the nematodes, because 98 per cent. of them survived. When one-quarter of the L.D. 55 dose was perfused, 94 per cent. survived. But with even only a very small dose of tetrachlorethylene (1 cc./ kgm.) only 20 per cent. of the nematodes survived, and the efficiency of 0·1 cc. of it was not impaired by the addition of 20 mgm. of sodium taurocholate.

The bulk of the nematodes were found in about 15 cm. of the small intestine about 20 cm. from the pylorus. Dosing caused them to move down the intestine, although their position was not greatly affected by tetrachlorethylene. Hyperperistalsis, induced by increasing the osmotic pressure of the medium in the

bath in which the perfused gut was studied (the apparatus enabled kymographic records of the intestinal movements to be made), did not displace the nematodes, although large volumes of fluid perfused loosened the mucus. But tetrachlorethylene freed the parasites from mucus, or stimulated them to enter the gut lumen, where many were killed. Not all nematodes killed by hexylresorcinol or tetrachlorethylene were passed immediately; some remained *in situ* and were digested 4 hours later.

The movement of the parasites down the gut was used to study the rate of action and relative activity of the two anthelmintics used. It was confirmed that hexylresorcinol is inactive against *N. muris* in the rat. The *in vitro* tests had suggested that it was inhibited by bile salts, by the rate of its passage down the gut, or by its rate of passage through mucin. These three factors were further studied. It was found that when they gained contact with the nematodes both hexylresorcinol and tetrachlorethylene probably acted rapidly. The fall in the killing rate after longer periods seemed to be due to the protection afforded by the mucus. In concentrated doses tetrachlorethylene acted rapidly, many worms being killed by it within one hour. This drug moved down the gut at a rate similar to that of a water barium meal and was often found 60 cm. from the pylorus after two hours. Thus anthelmintics must kill rapidly and at low concentrations to be effective in the short active gut of the rat. Phenothiazine, for example, which acts slowly and is efficient only in high concentrations, cannot affect *N. muris* unless its killing rate is artificially increased or its passage down the gut is delayed. Effective concentrations of it pass through the rat gut in one hour, while they require six hours to pass through the sheep gut.

Trim showed that 1 per cent. sodium taurocholate completely inhibits the passage of hexylresorcinol through the cuticle of *Ascaris lumbricoides*. Rogers found that 1 per cent. sodium taurocholate reduced the efficiency of hexylresorcinol against *N. muris* by 50 per cent. It was found that the concentration of taurocholate in the intestine of the rat varied from 0·6 to 1·3 per cent. half an hour after the dosing with hexylresorcinol. These figures may be low because infested rats seem to pass more bile salt; and ether, which depresses bile secretion, was used during the dosing and for killing. With larger doses the figures may be high because the soaps and resorcinol stimulate hepatic secretion. It was, therefore, concluded that the therapeutic dose of hexylresorcinol and sodium oleate may be inhibited 50 per cent. by bile salt. Adsorption of hexylresorcinol on to mucus reduces its concentration in the gut fluids and also prevents its penetration to the parasites in the mucus. These factors account for the inefficiency of hexylresorcinol against *N. muris*.

Trim found that low concentrations of sodium oleate increased the rate of penetration of hexylresorcinol through the cuticle of *Ascaris lumbricoides*. Rogers found that this also happens with *N. muris*; but at concentrations of 0·2 to 1 per cent. of sodium oleate, hexylresorcinol was inhibited, and at concentrations of 1 per cent. and upwards the soap alone killed the *N. muris*. Sodium laurate activated hexylresorcinol more effectively than did sodium oleate at *p*H 6·5 and this soap also had an anthelmintic action; but, at lower *p*H levels, the activity levels of oleate and laurate are reversed, so that in alkaline media oleate may be the more efficient against the nematodes.

The protective action of mucus was evident even though the perfusion loosened the mucus. Not only did the parasites seem to stimulate the secretion of mucus, but they were also found deep in mucus between the villi, so that they were well protected. Adsorption of hexylresorcinol on to mucus first occurred in the stomach and the small amounts reaching the small intestine were further reduced by adsorption on to the mucus there. The concentration of hexylresorcinol in the small intestine therefore probably only rarely reached levels

toxic to the nematodes. Additional causes of the drug's failure were its inability to perfuse through the mucus to the parasites and its poor ability to penetrate through the nematode cuticle, demonstrated by Trim. Its anthelmintic efficiency might be increased by : (1) reducing its adsorption on to mucus, *e.g.*, by giving it with an " enteric coating " insoluble in the stomach ; (2) reducing gastric and duodenal mucus with atropine ; (3) lowering mucus viscosity (ascorbic acid failed to do this in the author's experiments) ; (4) withholding food, which also adsorbs hexylresorcinol and stimulates the secretion of the inhibitory bile and mucus. The success of hexylresorcinol against other nematodes may be due to the ingestion by these parasites of mucus with hexylresorcinol adsorbed on to it. BROWN [this *Bulletin*, 1933, v. 30, 696] recorded, for example, the failure of hexylresorcinol against *Enterobius vermicularis* when it was given by the mouth. It probably failed for the reasons given above. But when it was given by enema and the inhibitory factors studied by Rogers and Trim were avoided, it succeeded.

The wide range of activity of tetrachlorethylene may be due to its relative therapeutic stability in gastric and intestinal fluids and to the fact that bile and mucus have little effect on it.

The anthelmintic action of detergents similar to the sodium oleate and laurate used by Rogers should be further studied. *G. Lapage.*

OLSEN, O. W. **Bionomics of the Lymnaeid Snail,** *Stagnicola bulimoides techella,* **the Intermediate Host of the Liver Fluke in Southern Texas.** *J. Agric. Res.* 1944, Nov. 15, v. 69, No. 10, 389–403, 4 figs. [24 refs.]

BAYLIS, H. A. **Tapeworm in Trout.** [Correspondence.] *Brit. Med. J.* 1944, Dec. 30, 868.

The author refers to the reports of DUGUID & SHEPPARD [this *Bulletin*, 1944, v. 41, 857], HICKEY & HARRIS [*ibid.*, 858], UNSWORTH (*Brit. Med. J.*, 1944, Sept. 16, 385), and HICKEY (*ibid.*, Oct. 7, 482). He has examined specimens sent to him by all these workers and concludes that those from gulls were of one species and those from the cormorant were of another species. On comparing adult worms, obtained experimentally in mammalian hosts by all the workers, he found that they all strongly resembled Hickey's species from gulls, and concludes that the experimenters were dealing with a single form, very probably an old but little-known species, *Diphyllobothrium dendriticum* (Nitzsch, 1824), normally a parasite of gulls. Slight differences might be the result of development in abnormal hosts (mammals). *J. F. Corson.*

ADDIS, C. J. & CHANDLER, A. C. **Studies on the Vitamin Requirement of Tapeworms.** *J. Parasitology.* 1944, Aug., v. 30, No. 4, 229–36.

Little work has been done on the vitamin requirements of cestodes. HAGER, Anne (*Iowa State Coll. J. Sci.*, 1941, v. 15, 127–153) found marked decrease in the egg production of *Hymenolepis diminuta* in rats kept on a diet deficient in vitamin " G-complex," but not when vitamin B_1 was deficient. CHANDLER [this *Bulletin*, 1943, 40, 705] found that *H. diminuta* is totally independent of the protein in the diet of the host and concluded that these cestodes obtained their protein by absorption direct from the host's mucosa and that this might explain the stunting of their growth by crowding. He also found that lack of vitamins in the host's diet, with or without the provision of protein, markedly affected the establishment of the worms in female rats, but not in male rats. For this reason the work here recorded was done with female rats only. Chandler's further work showed that this cestode is dependent on some factor

in autoclaved yeast in the host's diet, but that lack of the fat-soluble vitamins A, D, E, and of vitamin B_1 had no effect on the growth of the worms in female rats.

For the present investigation the method used in the author's earlier work was employed. Groups of female rats were taken and each rat was given 10 cysticercoids, reared by infection of the grain beetle, *Tenebrio molitor*. Rats were autopsied 14 days after infection, because then no segments are yet shed, although the cestodes have an average length as great as the length they attain later on. Details of the diets of the rats are given.

Experiment showed that lack of vitamins has some effect on the ability of the cestodes to establish themselves and on their growth, even when the host's vitamin reserves are intact, *i.e.* when the rats are put on deficient diets on the day on which they are infected. In experiment 2 the rats were allowed four days in which to use their vitamin reserves before they were infected. The result was that the number and size of the cestodes in the rats on deficient diets were reduced still further. The greatest stunting of the worms occurred in the groups lacking either all vitamins or only "G-complex" [riboflavin]. Lack of vitamins also definitely decreased the number of worms that established themselves.

In experiment 3 the rats were allowed 17 days in which to deplete their vitamin reserves before they were infected. The results showed that the effects of lack of vitamins were intensified. In the group whose diet was deficient in "G-complex," marked stunting of the cestodes occurred, while in groups getting adequate "G-complex" the cestodes grew longer than they did in the controls. This confirmed the view that these cestodes need for their normal growth enough "G-complex." The results also indicated that, without vitamins A, D, E and B_1, the cestodes grow larger rather than smaller. Absence of "G-complex" and of vitamins A, D and E also intensifies the reduction of the number of cestodes which establish themselves, but absence of B_1 does not.

Thus *H. diminuta* is dependent on "G-complex" in the host's diet; it is suggested that the cestode obtains it from the host's mucosa. The author is studying what components of the "G-complex" are concerned in this effect. Since the worms grow "in a perfectly normal manner" in the absence from the host's diet of any vitamin except "something associated with the G-complex," even after the host has depleted its vitamin reserves for a long period (17 days) it is suggested that the cestodes synthesize "these vitamins." The increase in the size of the cestodes in rats on diets deficient in fat-soluble vitamins agrees with the work of Ackert, McIlvaine, and Crawford (*Amer. J. Hyg.*, 1931, v. 13, 320–336), who found an increase in size of the nematode *Ascaridia lineata* in chickens on a diet deficient in vitamin A and attributed it to partial paralysis of the intestine and consequent richer flora in the intestine. This partial paralysis would allow *H. diminuta* to take up a more anterior position in the intestine, which would be more favourable to its growth (*cf.* the work of Burlingame and Chandler, *Amer. J. Hyg.*, 1941, Sect. D., v. 33, 1–21, on *Moniliformis dubius* of the rat), and this would explain why the cestodes grew to a greater size in the vitamin-deficient rats than in the controls.

The establishment of the cestodes in the gut seems to depend on proper evagination of the scolices and on their successful attachment. Evagination probably depends on the digestive juices and the *p*H, and Edgar (1941, *Trans. Amer. Microscop. Soc.*, 1941, v. 60, 121–128) suggests that proper secretion of bile would be necessary for evagination. [The toxicity of sodium glycocholate to scolices of *Taenia hydatigena* is discussed by de Waele (*Ann. Parasit. Humaine et Comparée*, 1934, v. 12, 492).] Possibly lack of vitamin A interferes with normal bile secretion and, if so, scolices might evaginate only near the entrance of the bile duct, and the others would be carried away. *G. Lapage.*

WHITELAW, J. C. G. & SANDY, F. **A Case of Infection of a European with** *Strongyloides stercoralis*. *J. Roy. Army Med. Corps.* 1945, Jan., v. 84, No. 1, 35.

SCHUBERT, R. Askariden-Cholangitis und -Pankreatitis. [**Cholangitis and Pancreatitis due to** *Ascaris*.] *Med. Klin.* 1943, Jan. 15, v. 39, No. 2, 34–7, 1 fig. [Numerous refs.

KING, B. G. **Early Filariasis Diagnosis and Clinical Findings : a Report of 268 Cases in American Troops.** *Amer. J. Trop. Med.* 1944, Sept., v. 24, No. 5, 285–98, 1 fig. [26 refs.]

[WARTMAN and KING (this *Bulletin*, 1944, v. 41, 860) published an abstract of this paper and the succeeding one (WARTMAN, below) before they appeared; the present papers give more detailed accounts.]

Clinical observations were made on 268 American soldiers who showed symptoms of filariasis after exposure to possible infection in Pacific islands during the period from May to September 1942; the author first saw them in January 1943.

Incubation period.—The earliest onset of symptoms was three months after arrival in the islands; a graph shows that in about 60 cases the incubation period was from 3 to 9 months, and in about 200 it varied from 10 to 16 months.

Mode of onset.—Only two patients had fever and headache at the onset; the first symptoms were pain, swelling or redness of an arm or leg, or pain and swelling in the scrotal region. The pain was never severe in the limbs and only rarely so in the scrotal region.

Clinical symptoms.—No cases of arthritis, hip-joint abscess, varicose glands, lymph scrotum, chyluria, chylous ascites, chylous hydrocele, chylous diarrhoea, or elephantiasis were observed. Fever occurred in 19·7 per cent. and was nearly always mild and lasted for a few days only. The syndromes could be classified in three groups: lymphangitis of the trunk or extremities; acute inflammation of the scrotum or its contents; and enlargement of lymph nodes. Relapses were frequent—one patient had lymphangitis six times—but acute local symptoms usually lasted for a few days only. No patient was seriously ill, but working efficiency was much interfered with.

Lymphangitis.—This was present in 51 per cent. and occurred most frequently in the arm; it took three forms—red streaks, patches of subcutaneous oedema and overlying redness, or diffuse oedema and erythema. As others have stated, it tended to extend centrifugally.

Genital lesions.—Inflammation of the spermatic cord, epididymis, testis, or scrotum occurred in 71·6 per cent.; funiculitis and epididymitis were the most frequent. The pain was sometimes exquisite.

Lymphadenopathy.—As others have noted, this was most frequent in the epitrochlear glands.

The blood showed eosinophilia in about two-thirds of the patients; one-quarter of them, however, had intestinal worms, chiefly *Necator americanus* and *Trichuris trichiura*. There was no leucocytosis. Microfilariae were not found in the blood though carefully looked for.

Diagnosis.—The author thinks that a clinical diagnosis is reliable; lymphangitis may be mistaken for thrombophlebitis, epididymitis for gonorrhoea, and funiculitis for hernia. The intradermal test described by TALIAFERRO and HOFFMAN [see this *Bulletin*, 1931, v. 28, 214] and by FAIRLEY [*ibid.*, p. 679] was used. Two antigens were made but one was found to be much more reliable than the other; it gave a positive reaction in 90·8 per cent. of the patients and in 10·5 per cent. of the controls. The author got strong evidence that positive

reactions were not produced by intestinal worms. From direct and indirect evidence he concludes that the patients were suffering from filariariasis due to *Wuchereria bancrofti.* *J. F. Corson.*

WARTMAN, W. B. **Lesions of the Lymphatic System in Early Filariasis.** *Amer. J. Trop. Med.* 1944, Sept., v. 24, No. 5, 299–313, 20 figs. [16 refs.]

This paper deals with material removed by biopsy from some of the cases of filariasis reported on by KING [above]. The material consisted of 20 lymph nodes and 4 cord-like structures from lesions of acute lymphangitis, removed from 17 soldiers. They had been exposed to infection for about four months in certain Pacific islands followed by five months in the Solomon Islands: it is very probable that they became infected during the former period. The specimens were eight epitrochlear, six axillary and six inguinal lymph nodes, three cords from the epitrochlear region and one from the axilla. Aerobic and anaerobic cultures from these specimens were negative. Semi-serial paraffin sections were examined and the findings are given in detail in a table and illustrated by photomicrographs. Adult male and female filarial worms were found in five specimens.

The lymphatic glands and vessels showed granulomatous inflammation around the worms, in the lymphatic sinuses, and in the capsule; these changes are described and figured. The worms were within enormously dilated cortical and medullary sinuses, and were surrounded by macrophages and reticular cells, with eosinophils and giant cells of the foreign body type. The lesions of the lymphatic vessels included proliferation of the endothelium and of the reticular cells, acute lymphangitis with or without thrombosis, and fibrous obliteration. Some worms were apparently alive at the time of biopsy and the tissue reactions around them were the same as those around dead worms. No free microfilariae were found. The author refers to a special article [this *Bulletin*, 1944, v. 41, 860] which was an abstract of KING's paper [above] and this one and to papers by FLYNN [this *Bulletin*, 1944, v. 41, 956], MICHAEL [*ibid.*] and HARTZ [*ibid.*, 955] as well as to earlier well-known publications on this subject. *J. F. Corson.*

BINGHAM, J. A. W. & MCDONALD, S. **A Filarial Nodule simulating a Cyst of the External Semilunar Cartilage.** *Brit. J. Surgery.* 1944, Oct., v. 32, No. 126, 326–7, 1 fig.

A cyst of *Onchocerca volvulus*, situated on the outer side of the left knee of a West African soldier, serving in India, was excised in mistake for a cyst of the external semilunar cartilage. It was found to lie between the capsule of the joint and the synovial membrane, exactly opposite the joint line in the middle of the outer side. The nature of the cyst was not suspected until paraffin sections were examined; though the species of filaria was not identified from the sections, there could be little doubt that it was *Onchocerca volvulus.* [Biopsy of the skin might have suggested or confirmed the diagnosis; see this *Bulletin*, 1923, v. 20, 945; 1924, v. 21, 214.] *J. F. Corson.*

TALICE, R. V. Estudios sobre la triquinosis. III. Cuándo debe el médico pensar en la triquinosis? [**Studies in Trichiniasis. III. When should the Physician think of Trichiniasis?**] *Arch. Uruguayos de Med., Cirug. y Especialidades.* 1944, Sept., v. 25, No. 3, 237–43. English summary.

"There is not a typical and uniform picture in trichinosis; only exceptionally does the physician encounter a really typical case of the disease; the patients show signs of very variable localisation.

"In the epidemic cases—whether great or small epidemic—the clinical diagnosis can be traced on epidemiological basis (ingestion of pork flesh) and the presence of common symptoms (especially oedemas of the face or other parts of the body, muscular pains, diaphragmatic signs, fever, loss of weight, digestive, hepatic and gastric signs, blood eosinophilia, etc.).

"In the sporadic cases, and on account of the endemic features of trichinosis in Uruguay, particularly in the rural zones, the physicians must think of that disease in all cases with high blood eosinophilia, oedemas, muscular pains, apparently allergic symptoms or diaphragmatic signs (pseudo-hepatic, pseudo-pleuritic, etc.) in the right side.

"The confirmatory diagnosis can be made only by laboratory methods and in specially trained services. In a next article I shall present a critical review about this aspect of the problem."

WRIGHT, W. H., JACOBS, L. & WALTON, A. C. **Studies on Trichinosis. XVI. Epidemiological Considerations based on the Examination for Trichinae of 5,318 Diaphragms from 189 Hospitals in 37 States and the District of Columbia.** *Pub. Health Rep.* Wash. 1944, May 26, v. 59, No. 21, 669–81.

This paper is reviewed in *Bulletin of Hygiene*, 1945, v. 20, 16.

HORNE, S. F. & HARRELL, G. T. **Trichinella Skin Tests in Patients in General Hospitals and Tuberculosis Sanatoria.** *Amer. J. Med. Sci.* 1944, June, v. 207, No. 6, 759–65.

This paper is reviewed in *Bulletin of Hygiene*, 1945, v. 20, 17.

DEFICIENCY DISEASES.

i. TROWELL, H. C. **Malnutrition in the Bantu of Central Africa. A Syndrome of Malignant Malnutrition.** *Clin. Proc.* Cape Town. 1944, Oct., v. 3, No. 8, 381–401, 10 figs. [14 refs.]

ii. BROWN, J. Scott & TROWELL, H. C. **Deficiency Bowel Pattern in Polish Refugees, African and Indian Adults and Children (Kwashiorkor).** *Lancet.* 1944, Dec. 23, 812–16, 2 figs.

i. In both articles will be found descriptions of the now well-known syndrome which in the past has been known as infantile pellagra but which subsequently was shown to occur in adolescents and adults. These accounts differ in no essential details from those already given by Trowell and others previously. The first article makes a most readable narrative and needs no further discussion except in regard to nomenclature. Trowell says "unfortunately, it is necessary to call the syndrome by a certain name, or it will be seldom diagnosed and treated. Such are the limitations of the human mind." He therefore calls it "the syndrome of malignant malnutrition." [His strictures on the limitations of the human mind are not perhaps without foundation; it is only necessary to recall the confusion which has arisen in vitamin nomenclature and which has occurred concerning some of the conditions ascribed to vitamin deficiencies. We like labels, they are useful, but would it not be wiser to wait till the pathogeny of the many deficiency syndromes has been worked out before attempting to give specific names to them. The expression "The syndrome of malignant malnutrition," it is suggested, is an unfortunate one—it is a title which surely should be claimed by pellagra, if for an instant the mortality of that disease, as it occurred last century in Italy and later in the endemic areas of U.S.A., be recalled].

The facts in regard to the condition under discussion appear to suggest a deficiency of calories, of protein and of vitamin B complex, including nicotinic acid and riboflavin : other factors in causation being helminthic and protozoal infections. [It is not clear, however, why the few develop the syndrome while others escape.]

ii. In the second paper the results are given of radiological examination of the gastro-intestinal tract, after the method of GOLDEN in U.S.A. (*Radiology*, 1941, v. 36, 262 ; *J. Amer. Med. Ass.*, 1941, v. 117, 913), in 16 cases comprising 2 Polish refugees, a nun, an Indian, 10 African labourers, all of whom had suffered dietary deficiency with a variety of symptoms, and 2 African children with symptoms of infantile pellagra.

The observations were mainly screen examinations. The appearances found were similar to those described by Golden and called by him the "deficiency pattern," but it was not seen in every case of gross deficiency state. [The authors apparently accept Golden's explanation of the "pattern" without comment, but it should be pointed out that the theory he put forward has been criticized by other workers.] *H. S. Stannus.*

SPIES, T. D., COGSWELL, R. C. & VILTNER, C. **Detection and Treatment of Severe Atypical Deficiency Disease.** *J. Amer. Med. Ass.* 1944, Nov. 18, v. 126, No. 12, 752–8, 4 figs.

The authors point out how much the "pattern" of the symptoms in "nutritive failure" may vary and how difficult it may be for the practising physician to recognize these patterns.

Ten cases are then recorded to illustrate the point, including : (1) A negro child, aged 5 months, who, after a severe infection (pneumonia), suddenly developed a watery diarrhoea and fiery red tongue, symptoms which responded to nicotinic acid in four hours. [It is not mentioned whether the child had received any sulphonamide drug.] (2) A white female, aged 33, with a history of restricted diet, associated with mental depression, but no stigmata of vitamin deficiency, who recovered rapidly with the exhibition of nicotinic acid. (3) A 67-year-old white female, complaining of intense "burning pain" in the soles of the feet, associated with an ill-balanced diet, which responded to an intravenous injection of 100 mgm. of thiamin. (4) A white male, aged 63, with pain in one eye and failure of vision associated with loss of weight, dizziness, weakness and nervous depression. The affected eye was injected and a small corneal ulcer was present. [Corneal vascularization is not mentioned ; presumably a slit-lamp examination was not made.] All the symptoms cleared up with riboflavin 20 mgm. intravenously, daily for two weeks. (5) A case showing sore mouth and tongue associated with diarrhoea, mental confusion and "burning feet" each year in spring and autumn, which responded to thiamin, etc. [Such cases, one believes, are commoner in Britain than is usually suspected. The occurrence of the syndromes of odd pattern should always be present in one's mind when investigating cases with a history of restricted diet or possible failure of absorption.] *H. S. Stannus.*

REMINGTON, R. E. **The Enigma of Pellagra.** *Southern Med. J.* 1944, Nov., v. 37, No. 11, 605–14, 7 figs.

The author says the "study of mortality and morbidity statistics [for pellagra] over a period of years reveals a number of facts which are difficult to interpret in the light of present day knowledge." Some of these are presented and discussed. They relate entirely to the endemic area in "the cotton belt" of the Southern States.

The author points out how, when the statistical data are "broken down", the original interpretation may be found to be misleading. There was a decline of 77 per cent. in pellagra mortality rates in 13 Southern States between 1928 and 1940. In South Carolina, where the death rate was higher than in any other area, the decline has continued through 1943, amounting to 91 per cent. of the rate in 1928, with a parallel drop in the incidence of the disease. This, the author shows, is due to some cause or combination of causes which affects the entire population, and not to remedial measures. Relief measures in the form of money or food in 1935 to 1938 had no effect.

The mortality among negroes is higher than among the whites but has decreased more rapidly; the means by which this population fraction, of the lowest economic status, has been able to make superior progress in eradicating pellagra is not clear, but possible explanations are suggested. It appears possible that some set of circumstances may have forced the population to produce or obtain by other means a greater variety of foodstuffs.

Attention is drawn to the difference between the sexes; the death rate in female negroes is 2·5 times as great as that in male negroes; in female whites 1·75 times as great as that in male whites.

The article is an interesting contribution to the epidemiology of pellagra.

H. S. Stannus.

FINNERUD, C. W. **Perlèche: its Nosologic Status.** *J. Amer. Med. Ass.* 1944, Nov. 18, v. 126, No. 12, 737–40. [31 refs.]

A discussion upon the several conditions due to a variety of causes which the author considers may be grouped together under the term "perlèche" and which he seems to believe cannot be diagnosed the one from the other.

[Finnerud fails to realize that the term was invented for a specific condition due to a specific cause. Presumably, therefore, it should not be used in a wider sense. The subject has already been dealt with in Britain by the reviewer, who puts in a plea that this foreign word should be suppressed. *Practitioner*, 1941, v. 146, 303; *Brit. Med. Jl.*, 1944, July 29, 140; *Lancet*, 1945, Feb. 3, 161.]

H. S. Stannus.

PETRI, S., NØRGAARD, F. & KIAER, W. **Studies on the Causation of Experimental Gastroprival Pellagra. IV. Therapeutic Experiments on Pig with Preventive Parenteral Administration of Vitamin B_6.** *Acta Med. Scandinavica.* 1944, v. 119, No. 4–5, 356–63, 3 figs. [10 refs.]

SEVRINGHAUS, E. L. **Adult Needs of Vitamins A and C.** *J. Amer. Med. Ass.* 1944, Nov. 18, v. 126, No. 12, 751–2.

The author believes that many individuals in the United States are not receiving a sufficiency of vitamins A and C, and refers to the difference in opinion as to optimum amounts per day. He thinks 15 mgm. of ascorbic acid and 5,000 I.U. of vitamin A approximately correct.

H. S. Stannus.

HAEMATOLOGY.

BROCK, J. F. **Recent Advances in the Aetiology, Terminology, and Classification of Anaemias.** *East African Med. J.* 1944, Oct., v. 21, No. 10, 298–309, 1 fig. [21 refs.]

This communication is an account of an address given before the Kenya Branch of the British Medical Association.

It comprises a survey of some recent views on the classification of anaemias on the basis of aetiology, together with a description of modern methods of studying the morphology of the peripheral blood in the diagnosis of anaemic states. Especial reference is made to recent work on tropical nutritional anaemias.

In the course of a preliminary consideration of normal haemoglobin levels and of the effect upon them of residence at high altitudes, the author states that iron therapy has a stimulating effect on erythropoiesis which is independent of its action in correcting deficiency. He argues consequently that conclusions based upon mass haemoglobin surveys may be fallacious, if the demonstration of the apparently sub-normal haemoglobin levels, which are found to rise after the administration of iron, be interpreted as necessarily indicating a pre-existing state of anaemia. *L. J. Davis.*

VENOMS AND ANTIVENENES.

BOQUET, P. Recherches sur le venin de *Dendraspis viridis*. [**On the Venom of** *Dendraspis viridis*.] *Bull. Soc. Path. Exot.* 1943, May 12 & June 9, v. 36, Nos. 5–6, 189–90.

The author has studied two specimens of dried venom from *Dendraspis viridis* sent from Kindia (French Guinea); they were light yellow in colour, and readily soluble in saline. The results of his investigations were :—

Specimen I.—A rabbit of 2,500 gm. injected with 1 mgm. (0·8 mgm. per kilo. body weight) shows progressive paralysis and death in asphyxia in 1½ hours. Guineapigs are less susceptible. Intravenous injection of 0·5 mgm. into an animal of 350 gm. (1·45 mgm. per kilo.) causes death in 15–20 minutes, while 1 mgm. subcutaneously kills in about 10 hours; smaller doses than this have no effect. Mice of 18–20 gm. die within an hour of intraperitoneal injection of 0·1 mgm. At autopsy, congestive, perhaps haemorrhagic, foci are found in the intestine.

Specimen II.—"This proved to be more toxic" says the author, but his records hardly bear this out; the difference was very slight. Intravenously 0·7 mgm. per kilo. killed a rabbit, and 0·1 mgm. killed a guineapig of 350 gm., and 1 mgm. subcutaneously was fatal to the latter animal (so was specimen I).

Attempts to neutralize the venom with antivenenes of *Naja tripudians*, *N. haje*, *Vipera aspis* and *Bitis arietans* were ineffectual. The action of the venom is thus like those of other African Colubridae, but is less powerful. Antivenenes for bites by Equatorial and West African snakes should therefore contain that for *Dendraspis* also as its antigenic properties are specific.

Madame PHISALIX in the discussion on this paper showed how the fangs of *Dendraspis* are long, and demonstrated, with the skull of *D. jamesoni*, that they are so disposed that the venom is introduced under pressure, like a dagger-thrust, into the depths of the tissues and that the elasticity of the tissues closes up the path of the fangs and the venom thus gains access rapidly to the bloodstream and symptoms begin to appear very soon after the bite. *H. Harold Scott.*

LINHARES, H. Variações da pressão arterial e liquorica apos inoculação de peçonhas de jararaca e cascavel. [**Variations in Arterial Blood-pressure and in the Cerebrospinal Fluid after Inoculation with Crotaline and Bothrops Venoms.**] Reprinted from *Jornal dos Clinicos*. Rio de Janeiro. 1938, Oct. 30, No. 20, 8 pp.

The author was desirous of finding out whether the results of the blood and spinal fluid pressures were the same, after inoculation of the venoms of *Crotalus*

and *Bothrops*, as Koressios had reported with that of *Naja tripudians*. Koressios had reported [the reference is not given] that after injection of 0·05–0·5 mgm. of cobra venom into the arm muscles of a healthy man no change worth noting occurred in these pressures, but that in the sick man there was an initial rise and a prolonged fall, less marked in the spinal fluid than in the blood.

The author used *Bothrops* venom (*Lachesis jararaca*) of a strength of 0·2 mgm. in one cc. and *Crotalus* venom (*C. terrificus*) of 0·1 mgm. per cc. The pressures were first taken and then the patient rested for a minute till he was quiet again and the pressures had settled to normal. Now 1 cc. of the venom preparation was injected intragluteally and in 5–10 minutes the pressure was again taken. As Koressios had found, the author observed no change in normal subjects in the c.s.f. pressure. No initial rise in arterial pressure was found to follow the intramuscular injection, only a prolonged fall ; slight rise followed intravenous injection of *Crotalus* or *Bothrops* venom, and the subsequent lowering of pressure was less with *L. jararaca* than with *C. terrificus*.

Twenty-six patients were the subjects of the tests, patients suffering from various nervous diseases : general paralysis, schizophrenia, imbecility, manic-depressive psychosis, etc., and the results of the pressures before and after the injections are given in a table. In the majority the blood-pressure was still low half-an-hour after the injection, more marked with the Crotaline venom. As regards the cerebrospinal fluid pressure, a fall of less than 4 mm. was present in three cases, of between 4 and 8 mm. in fifteen, and of more than 8 mm. in three cases. *H. Harold Scott.*

DERMATOLOGY AND FUNGOUS DISEASES.

MARCHIONINI, A. Beziehungen der Klimatologie und Ethnologie zur Entstehung von Hautkrankheiten in Anatolien. [**The Relation of Climate and Race to Skin Diseases in Anatolia.**] *Schweiz. med. Woch.* 1944, Aug. 5, v. 74, No. 31, 842–6, 9 figs.

The author started to practise in Ankara four years ago, after 16 years in a Skin Clinic in Germany. In the first few months he observed many cases of certain conditions which were new to him, except for mere textbook knowledge, and he came to the conclusion that, apart from the usual causes operating elsewhere, others of a climatic or ethnic nature must be taking a share.

Among such diseases the author mentions *cheilitis actinica* (of which he gives a photograph). This is an inflammation of the lower lip, and he saw a relatively large number of cases, some in an acute form, others more chronic with patches of leukoplakia. Sufferers rarely applied to the clinic for treatment. The disease was seen in the spring, but got much worse in the summer, was rare in the autumn and never seen in winter. Those attacked were mostly engaged in open-air employment—builders, peasants, coach-drivers, street-workers, for example. The condition started as small inflammatory swellings, later becoming vesicles, then eroding and crusting over. They were associated with a good deal of pain which made speaking and eating difficult. It was common for relapse to occur in successive summers. In the four years' work at the clinic at Ankara the author has seen 184 of these cases. He next enlarges on the temperature and humidity curves in Ankara and the district and demonstrates by charts the relations between these factors and the prevalence of the disease [but nowhere mentions the most probable explanation, that it is a pellagroid condition].

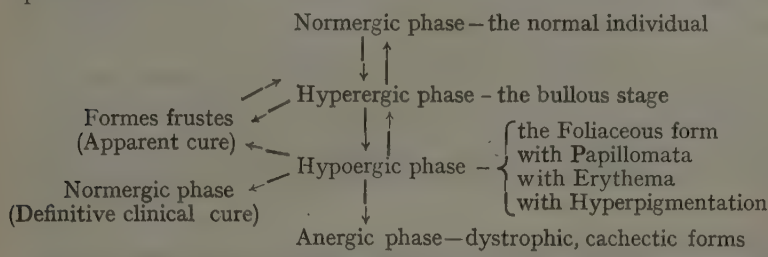
The author next speaks of *pyodermia* which in Ankara accounted for 32 per cent. of the applicants at the clinic ; in Jerusalem this is given as 34 per cent., as compared with 2–5 per cent. in other European countries. The Turks are

very cleanly and wash often. The disease is commonest in the summer, with high temperature and U-V rays abundant and powerful. The author ascribes as causative factors the prevalence of *Phlebotomus*, the dust nuisance, the reduction of the acid and diastase content of the skin (due to the high temperature and the U-V rays) and the transfer of pyococci from the fingers to the skin of the face and " the improved conditions for growth of bacteria there on account of the heat."

A note is added in conclusion on the rarity of certain other diseases, especially those affecting the genitalia; he mentions in particular balanitis, herpes, carcinoma of the penis, gangrenous or phagedaenic ulcer associated with Vincent's spirillum and *Fusiformis fusiformis*. *H. Harold Scott.*

TORRES, U. L. Conceito clinico do penfigo foliáceo brasileiro. [**Clinical Concept of the Brazilian Form of Pemphigus Foliaceus.**] *Arquivos de Dermat. e Sifiligrafia de São Paulo.* 1944, June, v. 8, No. 2, 86–125, 35 figs. [25 refs.]

Pemphigus foliaceus, the *fogo selvagem* or " wild fire " of Brazil, may be a truly terrible disease [see this *Bulletin*, 1927, v. 24, 451 ; 1943, v. 40, 487, 488]. The author maintains that the disease is not the same as the *Pemphigus foliaceus* of Europe ; the differences are important. In the first place, in Brazil it has two stages, an acute bullous or erythemato-bullous stage and a chronic exfoliative stage ; again, European cases rarely recover; in Brazil 10 per cent. (some say 15–20 per cent.) undergo spontaneous cure, and abortive *formes frustes* occur ; and it is seen in certain foci. The European disease is one of adults, in Brazil it is more common in adolescents and young adults and, finally, in Brazil the mucosae are never involved as they may be in the European form (though not often). The author's scheme of the development and phases of the disease is as represented here :—



The author suggests experimental work on the lines of injecting specific cytolysins, prepared from animal skin, based on the analogy of blood-sucking insects causing minute lesions and leading to the formation of cytolysins, and the action of streptococci which are invariably present in the lesions of this disease and play their part in keeping up the condition. Notes are given of thirteen cases with copious photographs depicting the disease in its different stages. *H. Harold Scott.*

STARLING, P. Sobre a etiologia alergica do penfigo(fogo selvagem). Nota prévia. [**Allergy as the Cause of Pemphigus (Wild Fire).**] *Brasil-Medico.* 1944, Aug. 5–12, v. 58, Nos. 32 & 33, 295–8.

The author calls attention to factors common to pemphigus and other allergic conditions as evidence that the first is also allergic; First, heredity, the frequency with which one or other parent is allergic; second, the disease is chronic "like asthma, epilepsy and eczema " ; third, the presence of eosinophilia ; fourth,

the records of spontaneous cure ; fifth, the likelihood of relapse ; sixth its non-contagiousness and absence of fever. He states that it attacks chiefly the poorer classes because they, more than others, live almost entirely on one sort of food—meat, beans, rice, flour, coffee—and those living in certain parts of the country because in those parts certain foodstuffs are grown almost exclusively. Among his patients were those allergic to coffee, milk, Guinea-grass (pó de capim), orange, French beans and manioc. He concludes by relating two cases cured, one " by a miracle," the other " by spiritism" as he calls them [by " penance " and by " pique " would be equally true]. The first was a man who had suffered from the disease for 15 years. He was a great meat-eater and as a penitential act vowed to abstain from meat for the future; his pemphigus cleared up. The second lived almost entirely on milk from his own cows. These failed and the city authorities introduced pasteurization and forbade the selling of non-pasteurized milk. In disgust, and saying that pasteurized milk upset his liver, he ceased to drink milk and his pemphigus began to clear up from that time. He had suffered from the disease for 20 years prior to this and he has now been free from symptoms for two years. [Not a very satisfying paper.] *H. Harold Scott.*

HATCH, W. E. & WELLS, A. H. **Actinomycosis of the Urinary Bladder complicating a Case of Madura Foot.** *J. Urology.* 1944, Aug., v. 52, No. 2, 149–52, 1 fig. [11 refs.]

After a compound fracture of the lower third of the right leg in a man aged 42, a condition of mycetoma developed. The disease, believed to be tuberculous, remained localized in the affected part, giving rise to much swelling and distortion of the foot, with sinuses discharging thick pus. Ten years after the onset of the mycetoma the man suffered a series of attacks of haematuria, each lasting two to three days. Two years later the haematuria became very severe and continuous and the patient was admitted to hospital suffering from the effects of haemorrhage from which he died 24 hours later.

At autopsy actinomycosis of the posterior wall of the bladder was discovered, and the foot lesion was found to be of a similar nature. Culture of the fungus was not obtained.

The case is of particular interest because actinomycosis of the bladder is uncommon, and metastatic spread of the disease from a mycetoma is extremely rare. *J. T. Duncan.*

FISHMAN, J. **Systemic Blastomycosis : with a New Form of Therapy.** *U.S. Nav. Med. Bull.* 1944, Oct., v. 43, No. 4, 758–61, 3 figs.

A woman, aged 19, was found to be suffering from blastomycosis (Gilchrist's disease), proved by isolation of the causative fungus *Blastomyces dermatitidis*, with involvement of the lungs, the bones of the tarsus and the skin. Surgical treatment, subsequent administration of sulphanilamide and sulphathiazole, regulated by daily determination of the drug concentration in the blood, for a month, and then intensive treatment with iodides by both oral and intravenous routes, and local treatment of the lesions with phenylmercuric nitrate, chemical coagulants and ultraviolet rays, were all without apparent good effect. [Presumably, vaccine treatment was not tried.] At this stage a " new treatment " was introduced, which consisted of the local application of ether to the skin and bone lesions, and internal administration by giving 4 oz. of ether in 4 oz. of oil by the rectum once daily on nine consecutive days. There was an early and marked improvement both in the local lesions and the general symptoms, and an X-ray examination showed a partial clearing of the lung shadows. The daily

ether administration by the rectum was resumed for a further seven days, and then once weekly up to the end of three months, when the patient was discharged from hospital, apparently cured. Confirmation of cure was obtained three years later when the patient died from the effect of an overdose of barbitone, and no evidence of the previous blastomycosis was found at the autopsy.

J. T. Duncan.

LEE, R. V. **Coccidioidomycosis in Western Flying Training Command.** *California & Western Med.* 1944, Sept., v. 61, 133. [Summary taken from *J. Amer. Med. Ass.* 1944, Dec. 2, v. 126, No. 14, 918–9.]

Lee says that all new personnel coming to the airfields are skin tested, and the negative reactors are retested six months later. All suspicious clinical cases in the dispensaries and hospitals are skin tested, and in addition specimens of blood are sent to the Army Epidemiological Board for confirmatory evidence when indicated. Over a quarter of a million skin tests have been given, a thousand or more clinical cases recognized and nine complete necropsies done. The author differentiates three forms of coccidioidomycosis: primary, intermediate and advanced. The primary form is usually subclinical. The only evidence of its having occurred is the finding of a positive skin test in an individual who was previously negative. This will occur in about 10 per cent. of personnel, but some stations have reported as high as 80 per cent. of the post population turning positive. Frequently, what would ordinarily pass as a cold, mild influenza or "desert rheumatism" is properly diagnosed as coccidioidal infection. When erythema nodosum occurs, the diagnosis is suspected much more frequently. The intermediate (or pulmonic) stage is the one which is most frequently recognized clinically. This is an acute, subacute or chronic pulmonary inflammation. It resembles tuberculosis. Cavities occur frequently, but they show a great tendency toward spontaneous closure. The advanced or disseminated form is about 100 times as likely to occur in the Negro as in the white soldier. Dissemination, if it occurs, is likely to occur early. If there are going to be late disseminations, the problem will be very difficult. In the disseminated cases almost every organ of the body has been involved; the body may be literally riddled with cold abscesses. There have been a few cases of dissemination in which apparent recovery occurred. That dissemination may be impending can often be anticipated from a rising titer in the complement fixation test. There is no effective treatment.

HEAT STROKE AND ALLIED CONDITIONS.

ALLEN, S. D. & O'BRIEN, J. P. **Tropical Anidrotic Asthenia: a Preliminary Report.** *Med. J. Australia.* 1944, Sept. 23, v. 2, No. 13, 335–6, 1 fig.

In the textbooks on tropical diseases a type of heat exhaustion is described in which there is said to be loss of diminution of sweating, but, in general, few details are given. This paper will therefore be quoted at some length, as it contains much that is new.

The description is based on 22 cases seen in Northern Australia and New Guinea. The patients nearly always gave a history of prickly heat, which had been extensive and severe; in most cases, however, it had disappeared three or four weeks before the loss of sweating began. Symptoms began insidiously, and were first noticed in the heat of the day; exercise produced an unusual degree

of exhaustion, together with dyspnoea, palpitation, headache, and giddiness. Some patients complained of a hot, tight, prickly feeling in the skin, and some at this stage noticed that they were sweating less than usual. At first the symptoms passed off with rest in a cool place, but, once established, they tended to recur more and more easily, and with greater severity, until exhaustion became extreme with the slightest exertion.

When examined during an attack, the patients were distressed and apprehensive, with a high pulse-rate (up to 140 per minute) and respiration rate (up to 46 per minute) and a moderately raised temperature (100–102°F. by mouth). There were characteristic changes in the skin. On forehead and face sweating was profuse ; the palms, soles and axillae were usually moist ; but elsewhere the skin was perfectly dry, rough and inelastic. On the trunk and arms, to a lesser degree on the forearms and legs, and rarely on the palms and soles, the skin seemed coarse, " like exaggerated gooseflesh." On close inspection the affected areas of skin were seen to be studded with greyish-white, papule-like elevations, which did not, as in gooseflesh, surround the hairs. They were about one millimetre in diameter, with no surrounding areola. On pricking with a needle, a minute drop of watery fluid could be obtained. The elevations were therefore vesicles, but deeper than those of dermatitis.

The arms and fingers, and less often the thighs, were sometimes swollen, with obliteration of the natural creases, but there was no pitting on pressure. In most cases the axillary and inguinal lymph-glands were moderately enlarged and tender.

No changes were found in the nervous system or blood-pressure. The amount and composition of the urine were, it is said, normal, though no figures are given.

With rest in a cool atmosphere the pulse-rate, respiration-rate, and temperature rapidly fell to normal. Full sweating was re-established more slowly. For ten to 14 days, symptoms and signs readily recurred on exertion. The only complication seen was impetigo of the face. In spite of the reduction in sweating, no case progressed to hyperpyrexia. No special treatment was adopted, apart from rest in a cool ward, and graded exercise in the cooler part of the day.

The histopathology of the skin was studied in serial sections of biopsy tissues. The changes are rightly described as of unusual interest : they occurred almost exclusively in relation to the sweat-glands and their ducts, and may be summarized as follows :—

(1) Occlusion of the mouth of the sweat-duct by a minute plug consisting of keratin and nucleated crescent-shaped cells.

(2) Formation of a small vesicle in the Malpighian layer by cystic distension of the occluded dust, which sometimes ruptured.

(3) Lymphocytic infiltration and dilatation of lymphatics round the duct immediately below the vesicle, in the papillary layer of the dermis.

(4) Dilatation of the whole lumen of the dermal part of the duct to two or three times its natural size.

(5) Moderate distension of the sweat-gland acini, with some degree of distortion and atrophy of the secreting cells.

(6) Accumulation of tissue fluid in the tissue spaces of the dermis, and dilatation of the lymphatics, especially round the sweat glands and their ducts.

(7) A slight degree only of vascular congestion.

(8) Blockage of hair follicles by a layer of keratin, resulting in distension of follicles with sebum, and atrophy of the hairs.

It is considered that the basic cause of the histological changes is the hyperkeratosis which occludes the ducts. Sweat is still formed, but cannot reach the

skin surface ; after bursting out of the ducts, it is reabsorbed by the lymphatics, and carried to the regional glands, which become enlarged. The general symptoms may result simply from the reduction in evaporative cooling in a climate where this is essential for the regulation of body temperature. On the other hand, the authors believe that part of the symptomatology is referable to the abnormal " internal circulation " of the sweat.

[In the past year (1944), in addition to this paper, two other descriptions have been published of heat exhaustion accompanied by reduction in sweating (WOLKIN, GOODMAN & KELLEY, this *Bulletin*, 1944, v. 41, 785 ; LADELL, WATERLOW & HUDSON, *ibid.*, 1945, v. 42, 143). This syndrome differs in almost every way from the classical type of heat exhaustion or prostration. Since it has not hitherto been clearly defined as an entity, it may be of interest to contrast the findings of the three groups of workers. In general they agree very closely, and this is noteworthy, since the work was done in regions as far apart as Northern Australia and New Guinea, the American desert and the desert of Southern Iraq.

In N. Australia the humidity is fairly high (70–80 per cent. relative humidity, with a dry-bulb of 80–85°F. (*Commonwealth Bureau of Meteorology, Melbourne, Bull. No. 14*, 1916) during the months when the cases occurred. In the desert regions the humidity is very low—about 30 per cent.—and the dry-bulb temperature reaches 120°F.

The symptomatology described by Ladell, Waterlow and Hudson in Iraq is almost identical with that recorded by Allen and O'Brien. Both groups of authors mention prickly heat as an antecedent ; both say that the prickly heat usually cleared up or improved before the onset of symptoms. In the reviewer's patients the onset of symptoms coincided with the disappearance of acute prickly heat, whereas in Allen's there was an interval of 2–3 weeks. Wolkin *et al.* make no mention of prickly heat, but say that loss of sweating was often preceded by a period of " distinct outpouring of sweat," lasting several days or weeks. In the Iraq cases, as in Allen's, the symptoms were brought on by exertion, particularly in the heat of the day.

All three clinical accounts agree on three important points : (*a*) that the body temperature was only slightly or moderately raised, in contrast to hyperpyrexia ; (*b*) that the skin was dry, and sweating appeared to be diminished, over part or all of the trunk and limbs ; and (*c*) that sweating was always profuse on the forehead and face. In hyperpyrexia these parts are dry, like the rest of the body.

There is some disagreement in the descriptions of the skin. Wolkin *et al.*, like Allen and O'Brien, say that it had the appearance of gooseflesh. They add that in cases of longer standing, there was a fine branny desquamation. Allen and O'Brien also found desquamation and ichthyosis, especially of the legs, in a few cases. In the reviewer's patients, in Iraq, the appearance described as gooseflesh was not seen ; the typical finding was desquamation, which was present to a varying degree in almost all cases. It was most severe on the legs, which were sometimes ichthyotic. Thus, although there are important differences, there are also certain common features in the three accounts.

All the authors agree that the general symptoms responded rapidly to rest in a cool place, but that normal sweating, and a normal condition of the skin, are restored more slowly. Impetigo and skin sepsis as a complication are mentioned by both Ladell *et al.* and by Allen and O'Brien. Both these groups point out that the diagnosis may easily be made of a functional nervous disorder, unless the condition of the skin is taken into account.

Wolkin *et al.*, produced objective evidence of reduction in sweating by comparing the sweat response to heat and to pilocarpine on admission and on recovery. Starch-iodine powder was used as an indicator. Ladell *et al.* showed that patients of this type had an abnormally high skin temperature, and were

unable, under some conditions, to maintain a constant body temperature. The American authors could not decide whether the failure of the sweating-response was due to a central or peripheral cause. Ladell *et al.* inclined to the view that the cause was peripheral, but, unlike Allen and O'Brien, they found no pathological changes in the sweat-glands. They did not, however, examine serial sections.

The syndrome described in Iraq contains one prominent feature which is not mentioned in either of the other accounts—polyuria. In some cases this amounted to 10 litres a day ; it began at the time of onset of the other symptoms, and often persisted for days or even weeks after admission to hospital. A thorough chemical investigation of these cases was carried out ; the only abnormality was a slight diminution in the chloride content of the plasma (about 90 milli Equiv. per litre) with a normal output of chloride in the urine. (In classical heat exhaustion, the urine contains no chloride.) In Wolkin's series, laboratory investigations were made in a few cases, but no reduction of plasma chloride was found. Wolkin and Ladell agree that salt had no beneficial therapeutic effect.

It will be seen that many points in this syndrome are still obscure. The practical importance of understanding and preventing this disease is emphasized by Ladell *et al.* In their material (soldiers in the desert) it was by far the commonest disability produced by heat, and, though not severe or dangerous, caused very great loss of time and efficiency.] *J. Waterlow.*

ELKINTON, J. R. & WINKLER, A. W. **Physiologic Effects of Drinking Undiluted Sea Water.** *War Medicine,* Chicago. 1944, Oct., v. 6, No. 4, 241–6, 4 charts. [Refs. in footnotes.]

The emphasis in this paper is on the physiological dilemma presented to the body when a man drinks hypertonic saline with a higher chloride concentration than can be excreted in the urine. Two things may happen, either the excess salt is excreted at the expense of body water, or it is retained ; the retention will involve a redistribution of body water, the extracellular fluid increasing at the expense of the intracellular. In a critical review of other authors' work on thirsting men, Elkinton and Winkler show that in all experiments there was a loss of body water and a hypertonicity of the body fluids when sea water was administered. These experiments on human subjects were all necessarily on the comparatively early stages of the condition ; but the present authors, using dogs instead of men, have been able to follow the changes until death. As dogs can excrete up to 3·5 per cent. NaCl in their urine, to produce the analogous experimental situation, 5 per cent. saline was administered.

When the strong saline was given to dogs in water balance the tonicity of the body fluids rose, and there was a shift of water from the intracellular to the extracellular phase ; when given to animals previously deprived of water for some time, some of the extra salt was eliminated, with the sacrifice of body water, but an increasing proportion was retained. The same shift of water into the extracellular phase occurred, and as a result the extracellular fluid volume remained adequate for the maintenance of the circulation, while the intracellular volume progressively diminished.

Death in these animals was not from circulatory but from respiratory failure, preceded by disturbances in the central nervous system. The authors consider that the few clinical descriptions in man of death after drinking sea water correspond to the picture seen in their dogs. They interpret the nervous changes as being due to the cells of the central nervous system participating in the general cellular dehydration.

In their discussion, they point out that the urinary volume during dehydration is largely determined by the urea to be excreted, hence it is not a good thing for thirsting castaways to subsist on fish. [The diuretic effect of protein and extractive during dehydration was taken into account in preparing *M.R.C. War Memorandum No. 8* (*Bulletin of War Medicine*, 1943, Apr., v. 3, No. 8, 463); this had been shown by experiment, and as a result it was advised that meat pemmican should no longer be issued in the emergency ration. The obligatory urine volume of 400 cc. per day taken as a basis for certain suggestions by British workers referred to men on the low protein diet recommended by the M.R.C.; with the pemmican diet higher volumes were found. As Elkinton and Winkler point out, on a completely nitrogen free diet very low urine volumes may occur.] *W. S. S. Ladell.*

RIEMERSCHMID, Gertrud. **Some Effects of Solar Radiation and other Factors of Climatic Environment on Human Beings.** *South African Med. J.* 1944, Nov. 11, v. 18, No. 21, 365–8.

Various scales of warmth which take into account other thermal factors besides air temperature are discussed. Some observations made in Johannesburg, Durban, Nairobi, and on the Island of Föhr, North Sea, with the "cooling-ball" or "frigorigraph" of Pfleiderer are recorded. This instrument takes into account air temperature, air velocity and radiation, but ignores humidity. [The records would have been of more value if there had also been given some information about air temperature and wind speed.]

Maximum and minimum temperatures at Davos, Belfast (S.A.), Kew, and Durban (S.A.) are also tabulated.

The main theme of the paper is that one or other of these special scales of warmth should be used when the physiological effects of meteorological conditions are being studied. *T. Bedford.*

i. JOKL, E. **Physiological Data showing that Standards of Physical Efficiency and of Heat Resistance of African Natives are High.** *Clin. Proc.* Cape Town. 1944, Sept., v. 3, No. 7, 355–6; 361–76, 8 figs. [17 refs.]

ii. ——. **Body-Weight as Determinator of Physical Efficiency.** [Correspondence.] *Nature.* 1944, Dec. 30, 830, 1 chart.

i. In experiments made by American workers, negroes performed standard work tests with heart rates several beats below those of white subjects, and the conclusion is drawn that this difference indicates a greater efficiency of energy transformation or of cardiovascular function on the part of the negroes. In maximal work tests the negroes attained higher maximal heart rates. Judged by the oxygen consumption during work the whites were less efficient than the negroes, allowance being made for body weight. The American investigators concluded that the trained negro of relatively pure racial stock is more skilful in walking and climbing than the white man, and that the negroes were able to use their oxygen debt to a greater extent.

Further studies carried out in humid heat showed that black subjects were superior to whites in various essential physiological adjustments. The negroes kept cooler than the whites, mainly because they produced less heat. Negro sharecroppers maintained lower body temperatures than any of the other groups studied.

Statistical evaluation of the results of physical efficiency tests conducted as part of the National Manpower Survey for South Africa indicates that among comparable groups of Bantu, Chinese, Cape Coloured, European and Indian

school children, Bantu children show on the whole the highest performances in running 100 yards (speed test) and 600 yards (endurance test).

In the Olympic Games members of the African races have scored several times as many successes as would be expected on the basis of their share of the world population. The Watussi tribe of Ruanda-Urundi in Central Africa produce outstanding high jumpers: hundreds of Watussi young men jump over 6 ft. and often 6 ft. 2 in. Record jumps of 7 ft. 2 in. are reported.

ii. The letter to *Nature* summarizes the results of a study of the effects of the body-weight of S. African schoolboys on their efficiency in three tests of physical fitness, *viz.*, (i) running 100 yards, which is taken to be a test of neuro-muscular skill and speed; (ii) running 600 yards, which tests circulatory and respiratory endurance; and (iii) putting the 12 lb. shot—a test of muscular strength. The 1,514 boys, of between 6 and 17 years of age, were divided into four groups according as they were underweight or overweight on the basis of Baldwin and Wood's age-weight tables. The boys in group A were underweight, *i.e.* 7 per cent. or more below normal; group B were slightly underweight, but less than 7 per cent. below normal; group C included the normal boys and those whose weight was less than 15 per cent. above the standard; while group D were boys weighing 15 per cent. or more above the normal.

In both the 100 yards and the 600 yards the extreme groups, A and D, that is the distinctly underweight and overweight groups, both put up performances that were significantly poorer than those of the intermediate groups. The performances of the intermediate groups did not differ significantly from each other in either test. In the 100 yards the poorer performances of the extreme groups did not differ significantly from each other; but in the 600 yards the fat boys of group D made a distinctly poorer showing than their fellows in group A.

In putting the shot the average performance increased progressively from group A to group D, but the differences between groups B and C, and between groups C and D, were not statistically significant. The one clear point here is that the underweight boys of group A put up a poorer performance than any of the other three groups. *T. Bedford.*

MISCELLANEOUS DISEASES.

TURNBULL, H. H. **Tropical Diseases in Returned Soldiers.** *Med. J. Australia.* 1944, Oct. 14, v. 2, No. 16, 397–401.

The author points out the difficulties which civilian medical officers in Australia may encounter in diagnosing and treating various tropical diseases in returning troops, owing to their unfamiliarity with these diseases. The most important of these diseases are malaria, dysentery and scrub typhus.

Malaria.—"The present routine course of treatment [details not given], followed by 0·1 gramme of Atebrin [mepacrine] per day for six weeks will produce cure of malignant tertian malaria in almost 100 per cent. of cases." This does not apply to benign tertian malaria but the course of mepacrine will postpone relapse. Every soldier who lands in Australia from New Guinea or other Pacific Islands is given a six-weeks' supply of the drug, and medical men should contradict the statements that it may cause sterility or damage the liver. Another point to remember is that malaria may give positive results in serum tests for syphilis.

Dysentery.—In New Guinea, sulphaguanidine produced "magical effects" in bacillary dysentery. Amoebic dysentery is much less common in New Guinea than in the Middle East; it exists also in Australia. The diagnosis and treatment are discussed and complications (hepatitis and liver abscess) are referred to.

Scrub typhus.—This was common among the troops in New Guinea and caused a number of deaths. It does not cause permanent damage to the heart, and patients usually recover in 4–6 weeks, occasionally after more than 4 months.

Schistosomiasis and *ankylostomiasis*—The former is uncommon, the latter common, in New Guinea. A single dose of 4 cc. of tetrachlorethylene, together with 1 cc. of oil of chenopodium, is recommended for ankylostomiasis; if necessary it may be repeated after ten days. *J. F. Corson.*

FAUST, E. C. **Diseases in the Tropical War Zones. V. The Diseases of the Far East, Southwest and South Pacific.** *Gastroenterology.* 1944, Sept., v. 3, No. 3, 163–87, 10 figs. [figs. 32–41.] [50 refs.]

In the fifth part of this series of papers the author treats the subject in the same way as in the earlier papers. In the section on malaria a useful list is given of the chief vectors, with their distribution and breeding places. The other diseases specially to be noted include amoebiasis, hookworm infection (including foci of *A. braziliense* in Malaya and the Philippines), clonorchiasis, filariasis, scrub typhus and plague.

[For earlier papers in this series see this *Bulletin*, 1944, v. 41, 966, 967; 1945, v. 42, 154.] *Charles Wilcocks.*

SOARES, T. Acêrca dalguns problemas de assistência relativos aos trabalhadores indígenas de África. [**Health Problems regarding African Labourers.**] *África Medica.* Lisbon. 1944, Aug.–Sept., v. 10, Nos. 8–9, 165–80, 3 charts.

The problems considered and the advice given in this contribution are such as are to be found in all works on tropical hygiene, but the article is useful as indicating the diseases prevailing in the Angola district.

Workmen before being engaged should undergo a physical examination and only those reaching a certain standard should be recruited; those accepted should be placed in camps under conditions as like as possible to those amid which they are going to work for "preparation and acclimatization" and they should be vaccinated against smallpox, enteric fevers, diphtheria and meningitis[but see later], be rid of intestinal and ectoparasites, and treated for any ailments from which they are suffering—malaria, yaws, trypanosomiasis [it seems hardly likely that a sufferer from trypanosomiasis would be accepted as a labour recruit]. If means of transport are not available the men should not march on foot "stages greater than 20–25 kilometres a day." Notes on housing, water-supply and food follow. In the Belgian Congo each labourer is given 500 gm. of meat, 600 gm. of manioc flour, 70 gm. of palm oil, 150 gm. of legumes and fresh fruit and 15 gm. of salt, or about 3,400 calories daily. They also eat fish and groundnuts, making up another 600 or so calories.

As regards provision for treatment of disease, it is suggested that hospital beds should be at the rate of 5 per cent. of the workers, and any hospital of 100 beds should have a dispensary for outpatients, place for small operations and a pharmacy; rooms for 3–4 beds each and a small maternity section; wards for isolation, rooms for disinfection, for baths, store for clothes, room for laundry and ironing, a kitchen, refectory and a mortuary.

The diseases chiefly met with are malaria, amoebic dysentery, ankylostomiasis, pneumonia (often very acute, ending fatally within 48 hours), yaws, venereal diseases, especially gonorrhoea, relapsing fever carried by *Ornithodorus moubata*, and sleeping sickness for which tryparsamide is used exclusively, in

doses of 0·03 gm. per kilo. body-weight, given in three series of 12 injections at weekly intervals, 3–4 weeks being allowed to elapse between the series. Variola and varicella are very common and at times become truly epidemic; tuberculosis, when it occurs, is of a severe type but it is not at all common among the native population, in fact it occurs mainly among those who come into contact with the whites. Though a certain number of cases of cerebrospinal fever are met with, the greater proportion of meningitis cases are pneumococcal in nature. Beriberi, both dry and wet forms, is fairly often seen; good results are obtained from the use of Betaxan and Benerva. Ulcers are very common, but quite good results are obtained with sulphonamides [the particular drugs employed are not mentioned]. *H. Harold Scott.*

SOYSA, E. & JAYAWARDENA, M. D. S. **Pulmonary Acariasis: a possible Cause of Asthma.** *Brit. Med. J.* 1945, Jan. 6, 1–6.

Another very interesting article confirming the findings of CARTER, WEDD and D'ABRERA [this *Bulletin*, 1945, v. 42, 73–74]. The present authors have seen a considerable number of cases (they record 30 in this paper) among Ceylonese soldiers. The characteristics in common were a high eosinophilia (40–80 per cent.), rarely any history of asthma or allergy in the family, absence, in most, of intestinal parasites, poor response to antispasmodics and ready response to arsenic. The ages of the 30 patients varied from 18 to 42 years and their length of service from three months to five years. Except for two who had had an attack of lobar pneumonia, none had suffered from any respiratory ailment. Twenty-five of the 30 had been on duty in connexion with ration stores, three others had worked in stores that were dusty.

The onset of the disease was slow and insidious, with intermittent dry cough, worse at night, and, later, attacks typical of asthma. The total leucocyte count ranged up to 37,000 per cmm. with high relative (and absolute) eosinophilia. In 11 out of 21 whose sputa were examined by the technique of Carter and his colleagues—a tedious process taking five days or longer—mites were found, *Tyroglyphus* or *Tarsonemus*. In six of the patients there was helminthic infestation, but treatment of this did not clear up the eosinophilia. X-rays revealed in the lungs linear striation and small discrete spots, particularly in the hilar and basal zones. All these disappeared promptly after arsenical treatment—carbarsone or stovarsol, two tablets daily for periods ranging from 6 to 33 days, and the response as a rule was rapid.

Diagnosis has to be made from: (1) *Tuberculosis*: No bacilli found and there is a ready response to arsenic. (2) *Pneumoconiosis*: The eosinophilia and response to arsenic. (3) *Bronchomycosis*: No hyphae and response to As. (4) *Cutaneous disease*: absent. (5) *Helminthiasis*: Absent (more commonly) or, if present, treatment does not affect the eosinophilia. (6) *Eosinophilic leukaemia*: Absence of immature forms of eosinophiles.

The finding of these cases opens up an interesting field for research as to how far and in what proportion of cases of Loeffler's syndrome and of "tropical eosinophilia" [see this *Bulletin*, 1941, v. 38, 538, 539; 1943, v. 40, 720, 721, 948; 1944, v. 41, 425, 517, 693] mites are present, and, next, how many of those recorded as suffering from the latter were really cases of pulmonary acariasis. [See also MANSON-BAHR & MUGGLETON, below, p. 325.] *H. Harold Scott.*

SMITHBURN, K. C. & HADDOW, A. J. **Semliki Forest Virus. I. Isolation and Pathogenic Properties.** *J. Immunology.* 1944, Sept., v. 49, No. 3, 141–57.

A virus was isolated from mosquitoes of the *Aëdes abnormalis* group, caught in the Semliki forest in Uganda. A mosquito suspension inoculated intracerebrally into mice produced paralysis in one animal on the 27th day; serial brain

passages were carried out, and the incubation period rapidly dropped to two days. The infection was invariably fatal, and by the 40th passage the average survival time was 48 hours. Mice could also be infected by intranasal, intraperitoneal and subcutaneous injection. The disease is characterized by paralysis of the hind legs appearing after 36 hours, followed by twitchings, convulsions and death.

After the 19th mouse passage the virus became virulent for guineapigs on intracerebral inoculation; virus of the 136th passage produced fever and paralysis in rabbits. Rhesus monkeys inoculated subcutaneously with the virus developed neutralizing antibodies without showing any evidence of disease.

The virus passed through Seitz EK filter pads, was not very sensitive to NaCl, and would withstand incubation for limited periods. It could be preserved by desiccation *in vacuo* with little loss of titre. The thermal death point was one hour at 60°C. After the intracerebral inoculation of mice, virus could be demonstrated in all parts of the body. The brain showed engorgement of blood vessels, perivascular cuffing and foci of necrosis. Lesions were also constantly found in the kidneys. *D. J. Bauer.*

SMITHBURN, K. C., MAHAFFY, A. F. & HADDOW, A. J. **Semliki Forest Virus. II. Immunological Studies with Specific Antiviral Sera and Sera from Humans and Wild Animals.** *J. Immunology.* 1944, Sept., v. 49, No. 3, 159–73.

Details are given of the methods of carrying out intracerebral neutralization and intra-abdominal protection tests with Semliki forest virus. By means of these tests the Semliki virus was shown to be distinct from the viruses of yellow fever, Bwamba fever, St. Louis and Japanese B encephalitis, and from the West Nile virus. An immunity survey was carried out on a total of 313 human sera collected in Bwamba county (in which Semliki forest is situated) and at localities on Lake Victoria 175 miles away. Sera from all localities showed neutralizing antibodies. Sera from 20 species of wild animals were also tested, and antibodies were found in six cases, all of which were primates; the results suggested that *Cercopithecus nictitans* might be the natural host of the virus. It is not yet known if this virus causes illness in man. *D. J. Bauer.*

BERMAN, C. **The Clinical Features of Primary Carcinoma of the Liver.** *Clin. Proc.* Cape Town. 1944, Sept., v. 3, No. 7, 323–30, 2 figs. on p. 360. [33 refs.]

The early diagnosis of primary hepatic cancer is notoriously difficult. The subject is well propounded and discussed in this paper by a leading authority. The fact that cirrhosis is a regular precursor is particularly interesting, for there is now much to show that cirrhosis of the liver is largely caused by malnutrition, and particularly by a deficiency of methionine. It seems to follow that by curing the dietetic fault we may be able to prevent, to some extent at any rate, both cirrhosis of the liver and its sequel of hepatic cancer.

Harold Burrows.

SCHNAKENBECK, W. Fischgifte und Fischvergiftungen. [**Fish-Poisons and Poisoning.**] *Münch. med. Woch.* 1943, Feb. 19, v. 90, No. 8, 149–51.

A useful reminder that all cases recorded as fish-poisoning are not so in fact. The author divides cases, as usual, into poisoning from the bite or wounds made by the spines and injected from poison-glands; that from eating the flesh or other parts which are intrinsically poisonous; and that from eating sound fish

which has become contaminated or undergone decomposition. He mentions single instances of these, but the value of the article lies in pointing out the danger of jumping to conclusions. Thus, he quotes the " mass poisoning due to fish " which was reported among the inmates of the casual ward in Berlin in 1911, when out of 162 inmates 71 died. Later investigations proved that the symptoms were due, not to fish, but to methyl alcohol. Again, an instance of poisoning from " smoked herrings " in a woman who had eaten of these. None others of the family were attacked and investigation of the case revealed that the woman had an attack of tonsillitis and suffered from " stomach trouble." When the symptoms of poisoning follow the eating of decomposed or bacterially contaminated fish, the cause should not be regarded as " fish-poisoning " in the strict sense of the term. The examples of true fish-poisoning which the author mentions are well known to readers of this *Bulletin*.

H. Harold Scott.

GENERAL PROTOZOOLOGY AND PROTOZOAL DISEASES.

LARSH, J. E., Jr. *Endamoeba invadens* **as an Aid in the Study of** *Endamoeba histolytica*. *Science*. 1944, Oct. 13, 342.

Because of its similarity to *Entamoeba histolytica* in both the free and encysted stages and its continued activity at ordinary laboratory temperature, the author advocates the employment of the reptilian *Entamoeba invadens* for class purposes. It may be obtained in culture from the General Biological Supply House. The processes of encystation, excystation and metacystic development resemble closely those of *E. histolytica*, while the disease produced, including invasion of the liver, in reptiles corresponds in essential features with amoebiasis in man. *E. invadens* was first described by RATCLIFFE and GEIMAN in 1934 (*Science*, v. 79, 324). Further details were given later (1936 and 1938) by these authors in two papers (*Parasitology*, v. 28, 208, and *Arch. of Path.*, v. 25, 160).

C. M. Wenyon.

GENERAL ENTOMOLOGY.

ANDUZE, P. J. Estudios de entomologia médica en el Estado Mérida (Venezuela). [**Studies in Medical Entomology in Venezuela.**] *Bol. Ent. Venezolana*. Caracas. 1943, v. 2, No. 3, 149–56. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 222–3.]

The results are discussed of investigations made in one district of the State of Merida, Venezuela, in September 1942 and in two others in August–September 1943 on diseases known or thought to be transmitted by Arthropods. They include malaria, which was first recorded in the State in 1926 and is spreading up the valleys from the lowlands as clearing progresses. The malarious zone is almost entirely rural. There is no indigenous malaria in towns situated above 3,100 ft., but nearly all the inhabitants of the lowlands have had the disease. The wet season is not well defined, and consequently there is no regular Anopheline or malaria season. *Anopheles argyritarsis*, R.-D., *A. eiseni*, Coq., *A. neomaculipalpus*, Curry, *A. pseudopunctipennis*, Theo., *A. strodei*, Root, and *A. oswaldoi*, Peryassú, were found at altitudes of up to 1,600 ft., the first four also at 1,600–3,300 ft., and *A. argyritarsis*, *A. pseudopunctipennis* and *A. boliviensis*, Theo., at 3,300–8,200 ft. *A. eiseni* was observed attacking man for the first time.

Except *A. strodei*, *A. oswaldoi* and *A. boliviensis*, the species taken are not considered as malaria vectors in Venezuela. However, in the absence of *A. albimanus*, Wied., and *A. darlingi*, Root, some of the species found must transmit the disease in the district. The catches included a large proportion of *A. oswaldoi*.

Relapsing fever is endemic in some parts at between 1,600 and 5,000 ft. and occurs cyclically. The vector, *Ornithodorus rudis*, Karsch (*venezuelensis*, Brumpt), is widely distributed. The cause of an epidemic that occurred in Tovar district in 1941, causing 37 per cent. mortality, and which might have been dengue or typhus, was investigated, *Aëdes aegypti*, L., was found in urban areas, and *A. argyrites*, Dyar and N. Tov., and females of two other species of *Aëdes* were taken in rural areas, but the disease was unlikely to have been dengue, in view of the high mortality and high altitude. Weil-Felix tests on 17 survivors gave negative results for OX19. However, it is possible that the rickettsia was one that does not agglutinate the Proteus used or that the failure to agglutinate was due to the lapse of time between the epidemic and the test. The possible vectors of a rickettsia disease were *Pediculus humanus*, L. (*corporis*, Deg.), *P. h. capitis*, Deg., and *Amblyomma cayennense*, F., *Cimex hemipterus*, F., and *Ornithodorus rudis* were abundant. The B-R [Briceño Rossi] rural test usually gave doubtful results, but was sometimes clearly positive; relapsing fever is endemic in the district, and Manson-Bahr has described a form with symptoms that agree with those of the disease under consideration and which had a mortality rate of 6 per cent.

Carate is undoubtedly present, and all infected persons examined gave positive reactions in the B-R test. In view of the suggestion that Simuliids are the vectors, many were caught; they included *Simulium lutzianum*, Pinto, *S. paraguayense*, Schrottky, *S. metallicum*, Bellardi, *S. bicoloratum*, Mall., and two species not yet determined. The limit of altitude for Simuliids appeared to be 7,500 ft. Yaws is widely distributed in some sectors of the district of Tovar. The B-R test again helped identification. Numerous Chloropids were collected, some of which are probably vectors of the disease.

It cannot be definitely said that Chagas' disease [caused by *Trypanosoma cruzi*] exists in Merida, but one patient had some of the symptoms. Two nymphs of *Rhodnius prolixus*, Stål, out of many of these bugs examined, had unidentified flagellates in the intestines. Cutaneous leishmaniasis is fairly common in the region of Estanques, and cases of the muco-cutaneous form sometimes occur. Sandflies (*Phlebotomus*) were found from the plains up to nearly 5,000 ft. and were abundant in some places.

SHER KHAN. **A Note on the Habits of *Eretes sticticus* L., a Predator on Mosquito Larvae.** *Indian J. Entom.* New Delhi. 1942, v. 4, Pt. 1, 90–91. [Summary taken from *Rev. Applied Entom.* Ser. B. 1944, Dec., v. 32, Pt. 12, 223.]

Observations at Delhi showed that adults of the Dytiscid, *Eretes sticticus*, L., occur in large numbers in stagnant water at the onset of the monsoon and lay their eggs singly in mud beneath the water, covering them with a foamy secretion. The egg, larval and pupal stages last, respectively, 3, 8–12 and 4–6 days in August. The larvae, which are very active when newly hatched, are predacious on mosquito larvae; a single individual destroys 350–400 during its development and as many as 100 in 24 hours when it is full-grown. Pupation takes place in a smooth cavity about three inches from the soil surface at the side of the pond.

HECHT, O. Algunos consejos técnicos para la cria de pulgas. [**Technical Advice on the Rearing of Fleas.**] *Rev. Sanidad Asistencia Social.* Caracas. 1943, v. 8, No. 6, 1163–5.

Abstracted in *Rev. Applied Entom.* Ser. B., 1944, Dec., v. 32, Pt. 12, 231.

PSHENICHNOV, A. V. & KHRAMUSHIN, J. E. [**Observations on the Seasonal Phenomena in the Life-History of *Ixodes persulcatus* in 1940, 1941 and 1942 within the Molotov Province.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 78. [In Russian.]

The authors summarize the results of field observations on the bionomics of the tick-vector of spring-summer encephalitis, *Ixodes persulcatus*, carried out in the course of three years in two forest districts of the Ural mountains. The ticks hibernate in all stages, except the eggs and unfed larvae, in the dead forest litter covering the ground. Hungry females and nymphs first make their appearance in the spring when the snow begins to thaw, while the mass emergence of females coincides with the beginning of foliation. There are two periods of oviposition, one at the beginning, the other at the end of June, while mass emergence of larvae is observed both in July and at the end of August and beginning of September. Hungry nymphs are found in large numbers at the end of April, the beginning of May, and the end of September. The different stages of the tick are encountered during the following periods: larvae, from the end of May to the first half of October, nymphs and adults ticks, all the year round, but the former are especially abundant at the end of April and the beginning of May, while the latter are most common at the end of May and beginning of June. *C. A. Hoare.*

PSHENICHNOV, A. V. & KHRAMUSHIN, J. E. [**Hibernation under Natural Conditions of *Ixodes persulcatus*, the Vector of the Spring-Summer Encephalitis.**] *Med. Parasit. & Parasitic Dis.* Moscow. 1943, v. 12, No. 5, 78–9. [In Russian.]

This paper deals with the results of experiments to determine the stages in which the vector of spring–summer encephalitis, *Ixodes persulcatus*, hibernates under natural conditions in the Ural mountains. Since the period of development of this tick varies considerably, all stages are available in winter. In the tests, various stages of development of the tick, both fed and starved individuals, were placed in test-tubes which were exposed in the forest on the surface or under the snow. Observations, made once a month in the course of the whole winter, showed that the eggs and unfed larvae all perish at −7 to −8°C., but all the other stages are capable of hibernating; provided the temperature does not fall below −28 to −30°C. Under local conditions, however, the temperature beneath the snow cover never reaches this level. The main habitat of hibernating ticks is provided by the forest litter, and is independent of the presence or absence of warm-blooded animals in the vicinity. *C. A. Hoare.*

MARTIN, R. Sur la pathogénie de la paralysie ascendante à tiques. [**The Pathogenesis of Ascending Tick Paralysis.**] *Arch. Inst. Pasteur d'Algérie.* 1944, June, v. 22, No. 2, 125–30.

i. WOMERSLEY, H. & HEASLIP, W. G. **The Trombiculinae (Acarina) or Itch-Mites of the Austro-Malayan and Oriental Regions.** Reprinted from *Trans. Roy. Soc. South Australia.* 1943, v. 67, No. 1, 68–142, 18 figs. & pls. II-XIII. [59 refs.]

ii. ——. **Notes on and Additions to the Trombiculinae and Leeuwenhoekiinae (Acarina) of Australia and New Guinea.** Reprinted from *Trans. Roy. Soc. South Australia.* 1944, v. 68, No. 1, 82–112, 14 figs. & numerous graphs.

i. The first paper reviews our knowledge of the larvae of the numerous species of "Harvest Mite" which attack man in many parts of the world, or transmit the infection of scrub typhus in Eastern and South Eastern Asia.

The authors find that it is only certain species of *Trombicula* which are vectors, though larvae of many species of this genus, and of *Eutrombicula*, *Schöngastia*, *Neoschöngastia* and *Leeuwenhoekia*, bite and irritate human beings.

It is evidently necessary for systematic purposes to complete the life history so as to relate a larva with certain characteristics to the corresponding adult. But this presents such great difficulties that at present 17 of the 19 genera of Trombiculinae, and a high proportion of the species, are known only from the larva. The authors point out that larvae are so small as to require the higher power of the microscope to identify them, and that it is difficult to do this while they are alive. On the other hand, it is not safe to assume that all larvae in one batch are of the same species, so that it is not justifiable to kill and identify some, and assume (*e.g.*, for transmission experiments) that the others are identical.

The authors describe their methods of study, and define a number of standard measurements. They recognise ten genera and 92 species of Trombiculinae from the Austro-Malayan and Oriental regions.

The paper contains keys to genera and species, and descriptions with figures of many species. A feature of the paper is the series of measurements of many individual larvae, which is given when material permits.

ii. The second paper is supplementary and gives statistical studies of standard measurements. Much of the material has come from the front in New Guinea.

P. A. Buxton.

MANSON-BAHR, P. & MUGGLETON, W. J. **Significance of Mites and their Eggs in Human Faeces.** *Lancet.* 1945, Jan. 20, 81–2, 1 fig. [18 refs.]

The commonest mites in foodstuffs and in faeces are cheese mites (*Tyroglyphus siro* and *T. longior*), the meal mite (*Aleurobius farinae*), and the housemite (*Glyciphagus domesticus*); there is much difference of opinion as to whether they are pathogenic or not. They were found in the faeces of Cornish miners by KHALIL [this *Bulletin*, 1922, v. 19, 120], in human urine by MACKENZIE [*ibid.*, 1923, v. 20, 47], and, recently, in the sputum of patients in Ceylon by CARTER and his colleagues [*ibid.*, 1945, v. 42, 73]. Manson-Bahr found them in faeces in 1921 and has seen them somewhat frequently during the past year; he recently saw various stages of development in freshly passed faeces of two people; the eggs somewhat resembled trematode eggs, but had no operculum and were much larger (0·1–1·2 mm. × 0·07 mm. [see below]) than ancylostome eggs. The development was watched under the microscope but it was difficult to identify the species; the authors think it was probably *Tyroglyphus siro*. The patient had had recurrent attacks of diarrhoea and had eaten quantities of over-ripe cheese in the Isle of Man. Neither of the two patients referred to had eosinophilia of over 5 per cent. The mites appear to have no pathological significance. [The dimensions of the tyroglyphid eggs given above are corrected in the *Lancet* of Jan. 27, 1945, p. 134; they should be 0·1–0·12×0·07 mm.]

J. F. Corson.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

GEORGETOWN, BRITISH GUIANA. **Annual Report of the Central Medical Laboratory, Georgetown, British Guiana for the Year ending 31st December, 1943.** [CLEARKIN, P. A.]. 13 typed pp.

A considerable extension of laboratory work is recorded; six clinical laboratories have been established and a large programme, involving training of technicians for other colonies, is proposed for the year 1944. A small booklet of technical methods was prepared during the year. The report contains some interesting observations and comments.

Malaria.—During the routine examination of blood films an unusually large number of gametocytes of *Plasmodium falciparum* was seen; enquiries were made and it was found that the same had occurred at the General Hospital, Georgetown. It seemed to be associated with treatment with mepacrine and investigations are being continued. The author suggests that the viability of the crescents should be tested in a non-malarious country where malaria therapy is practised.

Filariasis.—The early stage of filariasis was effectively treated by desensitization with an extract of *Dirofilaria immitis*; the number and severity of the attacks of fever, lymphangitis and oedema were reduced and health improved. Massage also was useful and the author advocates the establishment of a massage department. The skin test has proved valuable for diagnosis.

Syphilis.—The Laughlen test "has proved as reliable as the Kahn"; it requires much practice and experience to obtain consistent results. Technicians will be trained so that it can be done as a routine in all hospitals.

Allergic conditions.—The work on allergy continues; the author states that there is a great need for an asthma clinic. *J. F. Corson.*

SERGENT, Edm. Les Instituts Pasteur d'Outre-mer pendant la guerre. [**Pasteur Institutes Abroad during the War.**] *Arch. Inst. Pasteur d'Algérie.* 1944, June, v. 22, No. 2, 145–56.

AFRIQUE OCCIDENTALE FRANÇAISE. Rapport sur le fonctionnement technique de l'Institut Pasteur de l'Afrique Occidentale Française en 1942 (DURIEUX, C.]. [**Report of the Pasteur Institute of French West Africa for 1942.**] 86 pp. 1944. Dakar: Grande Imprimerie Africaine.

BLACKLOCK, D. B. **Metazoan Immunity.** *Lancet.* 1945, Jan. 20, 84–5.

The author refers to researches on the acquired immunity of hosts to various metazoan parasites, particularly worms and larvae of flies. He began such investigations on the larva of *Cordylobia anthropophaga* [this *Bulletin*, 1924, v. 21, 150; 1927, v. 24, 861; 1930, v. 27, 880]. This work having given successful results, he turned to the study of myiasis in cattle, caused by the warble fly, but, owing to various difficulties, little success was achieved. Meanwhile the study of metazoan immunity had been taken up by several American workers—TALIAFERRO [this *Bulletin*, 1931, v. 28, 214; 1932, v. 29, 45; 1934, v. 31, 818], MILLER [*ibid.*, 1931, v. 28, 205, 679; 1932, v. 29, 53, 415, 748], CULBERTSON and ROSE [*ibid.*, 1941, v. 38, 111; 1942, v. 39, 95; 1943, v. 40, 75, 77, 471, 794; 1944, v. 41, 770, 771; see also further references, this *Bulletin*, 1944, v. 41, 59, 223, 589, 764, 957, 952, 1054, 1055]. The author believes that, with our present greater knowledge of experimental methods and the recent advances in biochemistry, there is now a great opportunity for British workers to make discoveries in this field of research, which is of special importance in the tropics. *J. F. Corson.*

DILLON, R. A. **Native Medical Practices in the Southwest Pacific.** *New England J. of Med.* 1944, Nov. 23, v. 231, No. 21, 701–3.

SAL Y ROSAS, F. Hechos acerca de la influencia de los climas de altura y de la Costa del Perú en la Fisiología Nerviosa. Estudio experimental acerca de la susceptibilidad convulsiva de costeños y serranos.) [**The Influence of Mountain and Coastal Climates on the Nervous System: Experiments on the Susceptibility to Epileptic Convulsions of Coast and Mountain Dwellers.**] *Actualidad Méd. Peruana.* 1944, July, v. 10, No. 3, 51–5, 3 charts.

BOOK REVIEW.

KUDO, Richard R. [D.Sc., Associate Professor of Zoology, University of Illinois]. **Manual of Human Protozoa, with special reference to their Detection and Identification.** pp. ix+125, 29 figs. 1944. Charles C. Thomas: Springfield, Illinois; Baltimore, Maryland. [$2.00] [London Agents: Baillière, Tindall & Cox.]

Having been called upon to conduct emergency courses in which the methods employed for the detection and identification of protozoan parasites of man are studied, the author realized the need of a simple guide to the subject. Accordingly he has written this little book to help those who have to carry out this work. Only essential details have been given, and no attempt has been made to discuss the diseases produced, the pathological conditions associated with them, or the therapeutic measures adopted to bring about a cure. In fact the book deals only with the morphological appearance of the parasites and not with the physiological or pathological conditions. The true parasites, which are of necessity harmful, are 14 in number and comprise the trypanosomes, leishmania and malarial parasites, the dysentery amoeba, one ciliate, one coccidium and one sarcosporidian. The other protozoa, 13 in all, do not invade the tissues and are of doubtful pathogenicity. The structure, development and life histories of all these forms are carefully described and illustrated, and apart from certain minor details, the picture presented is an accurate one which cannot fail to be of assistance to those who are undertaking the study of the human protozoa for the first time.

After an introductory chapter there follow three on the protozoa parasitic in the digestive tract and one on the technique for their detection and identification. One chapter is devoted to the coprozoic protozoa which may appear in stale faeces and have often led to errors of diagnosis on the part of the uninitiated. In connection with the parasitic amoebae it is worthy of note that the author, despite the usual American custom, writes the generic name with a *t* instead of a *d* (*Entamoeba*, not *Endamoeba*) thus recognizing, as do all competent protozoologists, that the name *Endamoeba* Leidy, 1879 belongs to the amoeba of the cockroach, which is generically distinct from the parasitic amoebae of man and animals. It may be that the name *Entamoeba* should not be employed at all, but this is no excuse for forcing the human and many other parasitic amoebae into a genus to which they do not belong (see general discussion on this subject by DOBELL [this *Bulletin*, 1939, v. 36, 597]). The author's account of the intestinal amoebae is so good that it is perhaps a pity that the latest work of DOBELL on *Dientamoeba fragilis*, in which its flagellate affinities have been brought to light, has not been mentioned. Also in connexion

with technique a word or two on the subject of culture, which is of some diagnostic value, might not have been out of place. The intestinal flagellates are carefully described and it is interesting to note that the name *Retortamonas* is used for the name *Embadamonas*.

Chapter 7 is devoted to the trypanosomes and leishmania. As regards the former, the illustrations of *Trypanosoma gambiense* and *T. rhodesiense* leave much to be desired and they fail to depict the characteristic polymorphism of these organisms. The account of the leishmania is accurate, but more definite reference to the work on the transmission of oriental sore and kala azar by sandflies should have been made. In Chapter 8 the malarial parasites are dealt with and in Chapter 9 the technique for the detection of protozoa of the circulatory system. Chapter 10 is devoted to a consideration of "objects which may be confused with blood-inhabiting protozoa" but one would hardly have included in this category, as the author does, the normal white blood corpuscles. In the final chapter descriptions and illustrations of *Sarcocystis lindemanni* and *Trichomonas vaginalis* are to be found.

The author's method of writing the scientific names does not conform to the rule: thus he gives *Trichomonas vaginalis* Donne 1837, without a comma between the Donne and the date. This omission occurs all through the book. In some places the English wording is peculiar, there being a tendency to the dropping of the article where it would be expected. In other places it is quite ungrammatical. However, these are small points which do not detract from the excellence of the book, which is remarkable for the high standard of its printing, paper and binding alike. It is undoubtedly an artistic production and it seems a pity that those who produced the book did not read it more carefully before passing it.

The book, as already noted, will be useful to those who are taking up the study for the first time and want no more than a bare outline of the subject.

C. M. Wenyon.

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